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# CORTICAL MOTOR MECHANISM OF THE SHEEP BRAIN *

CHARLES BAGLEY, JR., M.D.

BALTIMORE

## INTRODUCTION

This paper is a part of a general study of the entire cortex of the sheep brain, the motor area alone being considered in this communication. The work has been carried on under the direction of Dr. Adolf Meyer, to whom I am grateful for guidance and much valuable assistance.

Marcacci,[1] in 1877, outlined in the sheep brain four excitable areas: first, the center for the opposite fore limb in the posterior part of the superior frontal convolution; second, the center for the muscles of the neck, stimulation of which caused the head to pull to the opposite side and in the male, a movement simulating butting; this center he also located in the superior frontal convolution in front of that for the fore limb; third, a center for movements of the facial muscles; no mention is made concerning whether these movements occur on the same or opposite side. He frequently noticed that associated with the movements of these muscles there were movements of the tongue. This area was located toward the outer side of the coronal sulcus, toward the anterior pole of the brain, in very much the same position as the center for movements of muscles of the same side of the face as determined by our stimulation experiments. On the extreme frontal pole of the brain at the anterior extremity of the coronal sulcus, he located the fourth center, that for movements of the mandible, stimulation of which caused movements of the jaw, simulating chewing.

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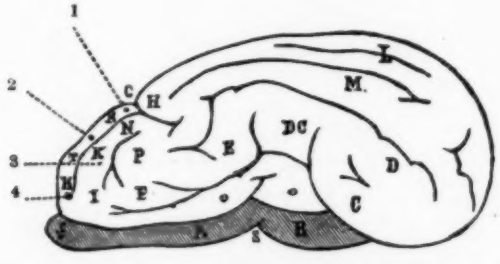
* From the Neurological Laboratory of the Henry Phipps Psychiatric Clinic, Johns Hopkins University.

* Read before the Forty-Seventh Annual Meeting of the American Neurological Association, Atlantic City, N. J., June, 1921.

1. Marcacci, A.: Determinazione della zona eccitabile nel cervello pecorino, Arch. ital. per le mal. nerv., Milano **14**:34-38, 1877.

Ziehen [2] found that a center for movements of the opposite fore limb was in the superior frontal convolution, just anterior and posterior to the fissura splenialis and that for the hind limb was posterior to the cruciate sulcus (area perpendicularly shaded in Figure 2). Stimulation of the cortex lateral to the coronal sulcus resulted in raising the head, crossed shoulder movements and turning the head to the opposite side.



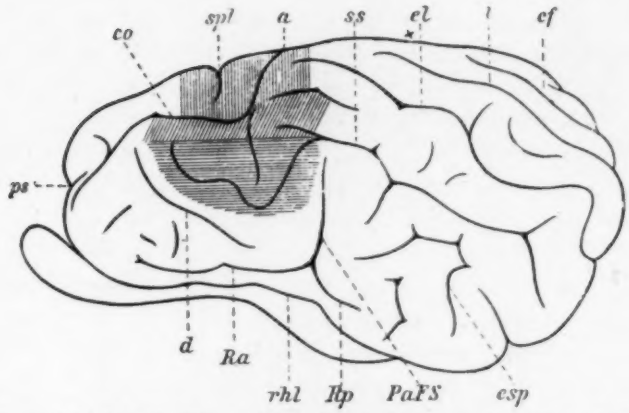

**Cervello di agnello veduto nella sua faccia laterale sinistra.**

*c.* Scissura crociata.
*s.* Scissura Silviana.
*o. o.* Lobo dell' insula, allo scoperto.
*B.* Lobulo sfenoidale o mastoide.
*A.* Circonvoluzione olfattiva.
*f.* Bulbo olfattivo.
*D. C. E. P. F.* Circonvoluzioni temporali.
*L. M.* Circonvoluzioni occipitali.
*H.* Circonvoluzione parietale posteriore, post-crociata.
*R. N. T. K.* Circonvoluzioni parietali anteriori pre-crociate.
*I. II.* Circonvoluzioni frontali.
1. Centro motorio di flessione per l' arto opposto anteriore.
2. Centro motorio della cervice, e di cozzo.
3. Centro motorio della faccia e della lingua.
4. Centro motorio mandibolare.

Fig. 1.—Motor areas of the cortex of the sheep brain, after Marcacci.

This area like that for the hind limb extends behind the cruciate sulcus (area obliquely shaded in Figure 2). Stimulation of the cortex just lateral to this area, in the anterior region of the sulcus suprasylvius

2. Ziehen, T.: Ein Beitrag zur Lehre von den Beziehungen zwischen Lage und Function im Bereich der motorischen Region der Grosshirnrinde mit specieller Rücksicht auf das Rindenfeld des Orbicularis oculi, Arch. f. Anat. u. Physiol.; Phys. Abt., 1899, pp. 158-173.




Laterale Convexität des Schafhirns. Linke Hemisphäre, von der Seite und oben gesehen. *a* = „Bügel *a*", *cf* = Sulcus confinis, *co* = S. coronalis, *d* = S. diagonalis, *el* = S. ectolateralis, *esp* = S. ectosylvius posticus, *l* = S. lateralis, *PaFS* = Processus acuminis Fossae Sylvii, *ps* = Sulcus praesylvius, *Ra*, *Rp* = Ramus anterior bezw. posterior der Fossa Sylvii, *rhl* = Fissura rhinalis lateralis, *spl* = Einschnitt der Fissura splenialis. *ss* = Sulcus suprasylvius. Bei × zieht eine grosse Vene über die laterale Convexität. Die Bedeutung der Schraffirungen ist im Text nachzulesen.

Fig. 2.—Motor areas of the cortex of the sheep brain, after Ziehen.

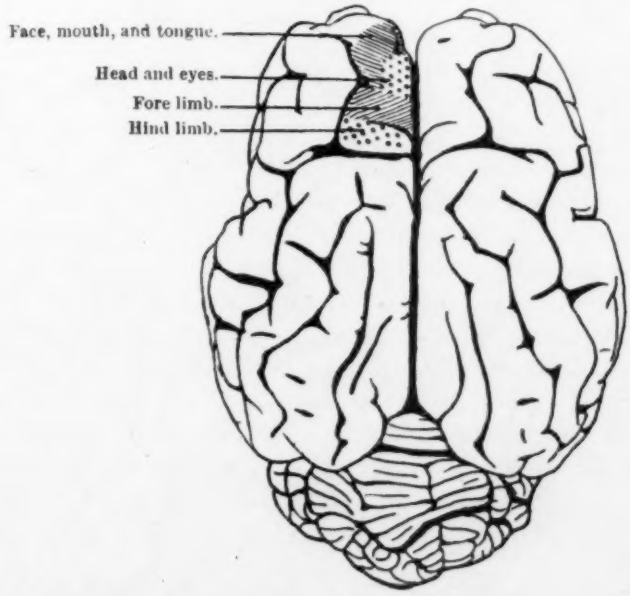



Fig. 3.—Motor areas of the cortex of the sheep brain (dorsal aspect), after Simpson and King.

behind the sulcus diagonalis, gave contractions of the mouth, eye, ear and face musculature of the opposite, and later also of the same side (area horizontally shaded in Figure 2). Somewhat behind the sulcus diagonalis he obtained contraction of the mouth-face muscles only; behind the latter area he found decided movements of the crossed ear and the crossed orbicularis oculi; contractions on the same side were not noticed. In this area he noticed a marked flow of saliva and sometimes mastication and movements with extension of the tongue (Fig. 2).

Several years later, Simpson and King [3] performed twenty-three experiments and concluded that the cortical motor area was located in the superior frontal convolution, that it extended from a line 2 mm. in front of the cruciate fissure behind to almost the frontal pole of the hemisphere, and lateromesially from the coronal sulcus over the mesial

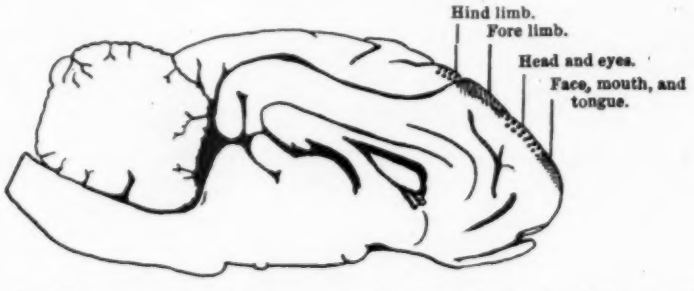



Fig. 4.—Motor areas of the cortex of the sheep brain (mesial aspect), after Simpson and King.

border, about 1 mm. on the mesial aspect of the hemisphere. They outlined four areas from behind forward for the hind limb, fore limb, head and eyes, and face, mouth and tongue, and concluded that the latter was the least excitable. In many individuals, motor responses were not obtained from one or more of these areas (Figs. 3 and 4).

Leonardo Bianchi [4] located the center for the movement of the posterior and anterior limbs in the posterior portion of the superior frontal gyrus and that for the muscles of the neck and trunk, just anterior to these centers. To the outer side of the coronal sulcus in the posterior extremity of the midfrontal convolution, just anterior to the cruciate sulcus, he located the center for the opening of the eyelids. In the cortex just posterior to the cruciate sulcus, he located

3. Simpson, S., and King, J. L.: Localization of the Motor Area in the Sheep, Quart. J. Exper. Physiol. **4**:53-65, 1911.

4. Bianchi, L.: La meccanica del cervello e la funzione dei lobi frontali, Torino, F. Bocca, 1920.

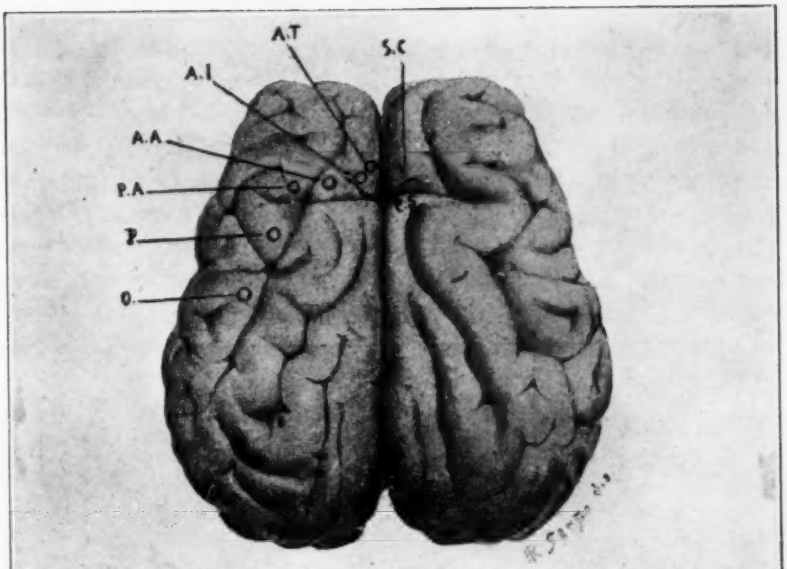



Fig. 38.

**PS. Polo sagittale. — SC. Solco cruciato. — AT. Area di eccitazione della muscolatura della nuca e del tronco. — AI. Idem per l'arto posteriore. — AA. Arto anteriore con movimenti meno evidenti dell'arto posteriore. — PA. Apertura delle palpebre. — P. Chiusura delle palpebre. — O. Movimenti dell'orecchio.**

Fig. 5.—Motor areas of the cortex of the sheep brain (dorsal aspect), after Bianchi.

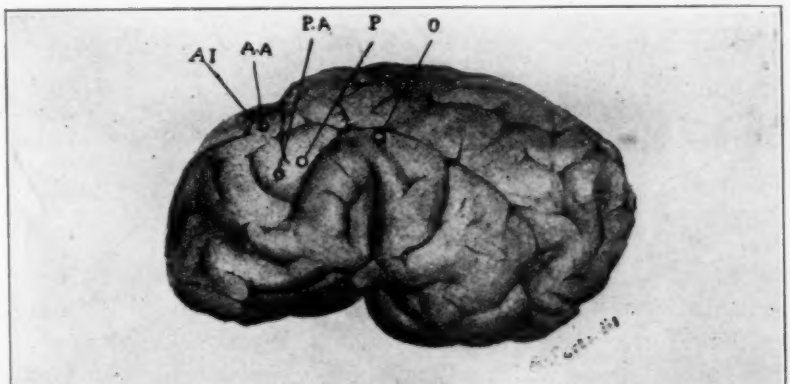



Fig. 39.

**O. Area per i movimenti dell'orecchio. — P. Chiusura delle palpebre. — PA. Apertura delle palpebre. — AA. Movimenti dell'arto anteriore e un po' meno evidenti dell'arto posteriore. — AI. Movimenti dell'arto posteriore e un po' anche dell'anteriore.**

Fig. 6.—Motor areas of the cortex of the sheep brain (lateral aspect), after Bianchi.

the center for closing the lids. Immediately lateral to the suprasylvian and opposite the upper extremity of the sylvian fissure, he located the center for movement of the ear (Figs. 5 and 6).

The course of the fibers from the motor cortex to the spinal cord was investigated by Dexler and Margulies,[5] who studied the pyramidal tract of the sheep in Marchi preparations after extirpation of almost an entire hemisphere. King[6] studied the pyramidal tract after extirpation of areas varying from the cortex of the superior frontal convolution alone, which she determined to be the excitable cortex (Figs. 3 and 4), to the areas in which the adjacent convolutions also

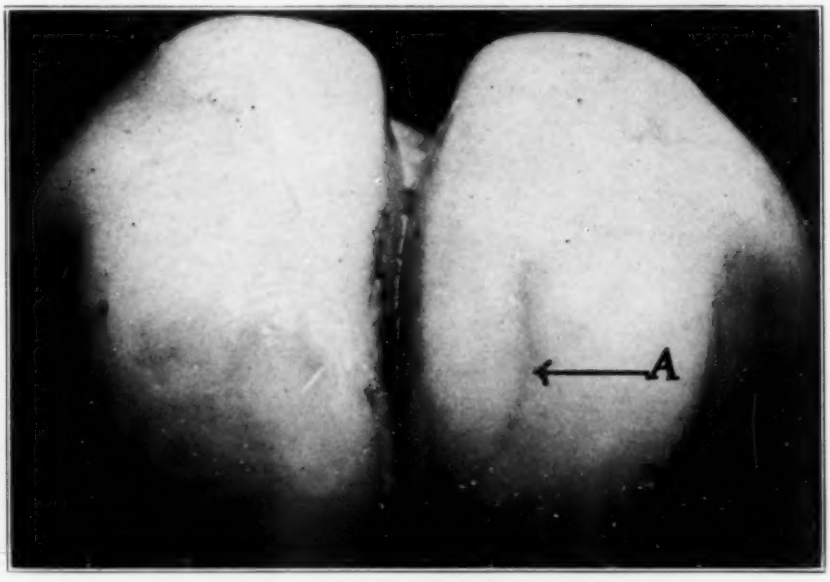



Fig. 7.—Frontal pole of the brain of the 15.5-cm. sheep embryo, showing the coronal sulcus at *A*, which marks the first indication of the motor area.

were destroyed. King concluded that the pyramidal tract of the sheep was comparatively small; that the fibers of the pyramidal tract decussated in the lower part of the medulla and first cervical segments of the cord; that they could be traced into the reticular formation at the base of the dorsal horn and among the lateral horn cells as well as those of the dorsal part of the ventral horn. This was also true of the homolateral fibers. The tract could not be traced beyond the first

5. Dexler, H., and Margulies, A.: Ueber die Pyramidenbahn des Schafes und der Ziege, Morphol. Jahrb., Leipzig **35**:413-449, 1906.

6. King, J. L.: The Pyramid Tract and Other Descending Paths in the Spinal Cord of the Sheep, Quart. J. Exper. Physiol. **4**:133-149, 1911.

cervical segments. An uncrossed ventral corticospinal tract could not be demonstrated.

King in describing the course of degeneration in sections made at various levels of the brain stem made no mention of degeneration extending into the tegmentum.

Dexler and Margulies [5] in their study of Marchi preparations of the midbrain, after extirpation of almost an entire hemisphere, mentioned an area of very fine degeneration which turned laterally and dorsally in the midbrain and was lost. They concluded that because of the great areas of softening which affected the thalamus after their

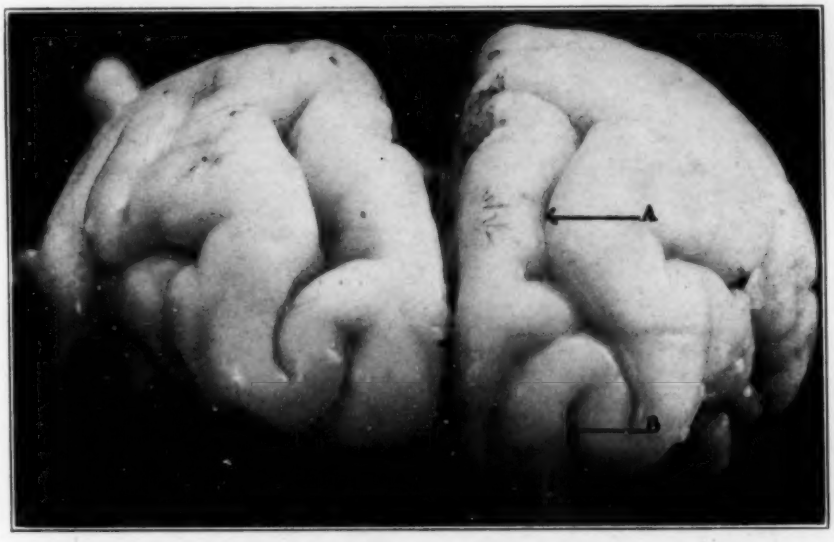



Fig. 8.—Frontal pole of the brain of the 30-cm. sheep embryo, showing the coronal sulcus *A*, with its various spurs and the anterior end of the presylvian sulcus *B*.

extirpation, a definite statement concerning this degeneration could not be made. They also noticed a coarsely degenerated bundle, the fibers of which seemed to go through the raphé to the opposite side. The latter bundle and the preceding one fell outside their consideration, as the fibers did not reach the cord.

Dräseke [7] in Marchi preparations of the midbrain of *Vesperugo serotinus* and *Pteropus ursinus* described a "proximal crossing" of the pyramidal tract and suggested that the fibers of this bundle were distributed to the nuclei of the motor cranial nerves. Merzbacher and

7. Dräseke, J.: Zur mikroskopischen Kenntnis der Pyramidenkreuzung der Chiropteren, Anat. Anz. **23**:449-456, 1903.

Spielmeyer [8] in work done on *Vesperugo noctula*, corroborated this finding, although they were in disagreement with Dräseke on other points.

Simpson,[9] in describing a frontal section of the midbrain at the level of the anterior corpora quadrigemina in Marchi preparations after

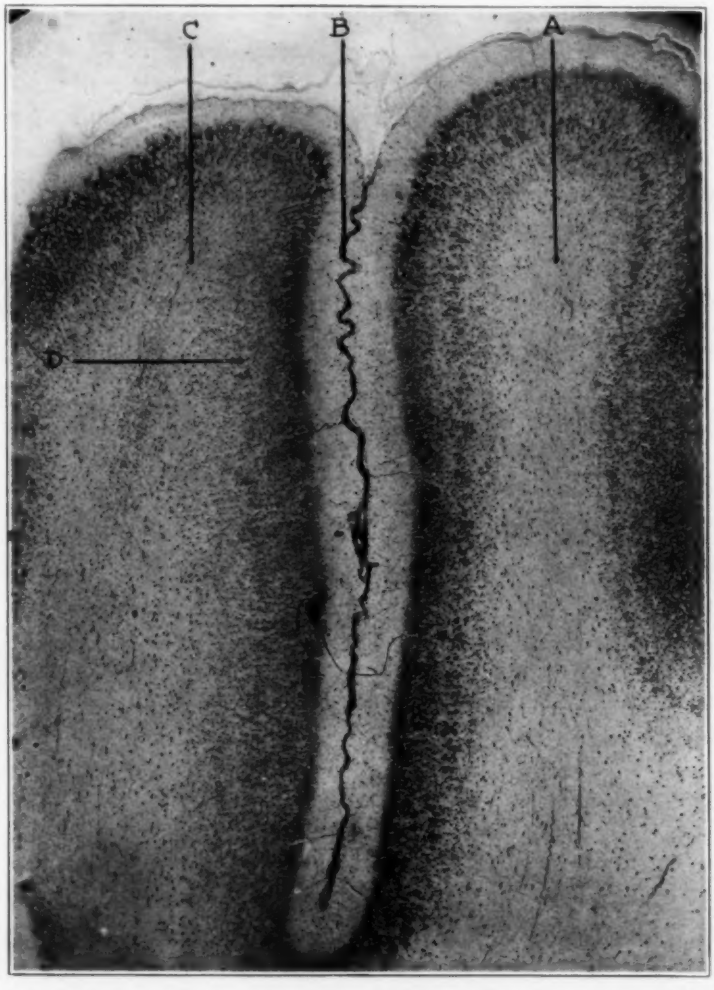



Fig. 9.—Section through the motor area of the 30-cm. sheep embryo: *A*, superior frontal gyrus; *B*, coronal sulcus; *C*, middle frontal gyrus. The layer of large pyramidal cells which extends throughout the superior frontal gyrus and stops abruptly in the middle frontal gyrus at *D* may be noted.

8. Merzbacher, L., and Spielmeyer, W.: Bieträge zur Kenntnis des Fledermausgehirns, besonders der corticomotorischen Bahnen, Neurol. Centralbl. **22**: 1050-1053, 1903.

9. Simpson, S.: The Motor Areas and Pyramid Tract in the Canadian Porcupine (Erethizon dorsatus, Linn.), Quart. J. Exper. Physiol. **8**:79-102, 1915.

extirpation of the motor cortex in the brain of the Canadian porcupine (*Erethizon dorsatus,* Linn.), mentioned small fiber bundles cut transversely behind the main mass of the pyramid and running parallel with it. He also mentioned other fiber bundles which came off from the dorsal aspect of the crusta and passed backward into the tegmen-

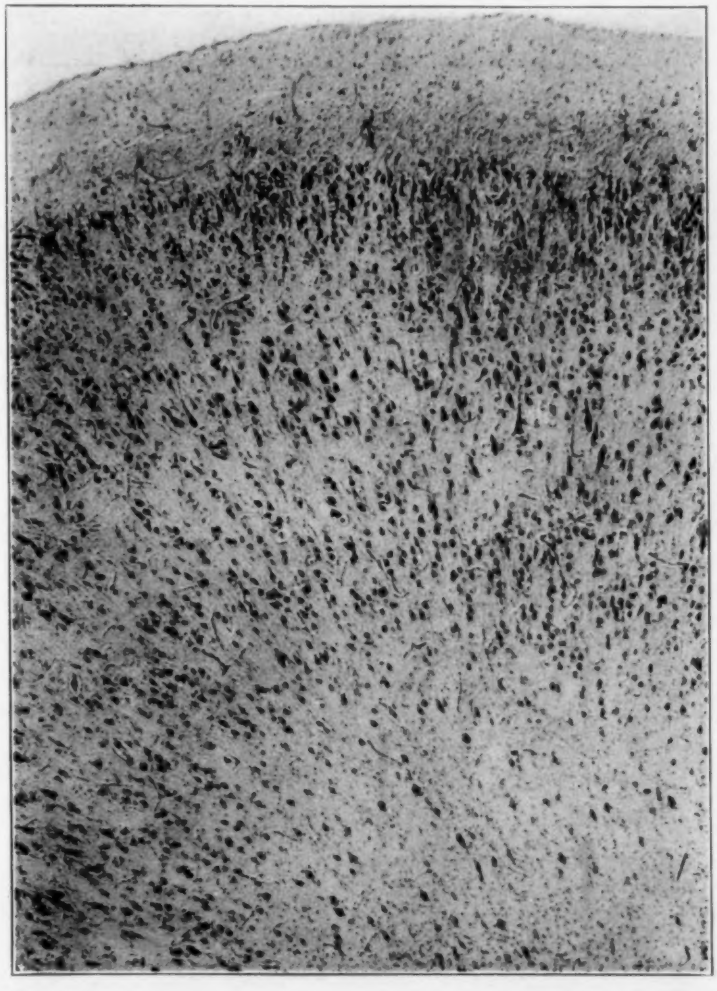


Fig. 10.—From the motor cortex at Area 1 in Figure 17. The first layer is relatively broad; the second layer is rich in cells, while the area between this and the layer of large pyramidal cells is narrow, indicating the absence of the granular layer. The large pyramidal cells are present in greater number than in other parts of the cortex; × 80.

tum at right angles to the main mass of the tract. These fibers, he believed, terminated in the gray matter somewhere in the vicinity; but they could not be traced to any particular nuclei.

Bregmann,[10] working with sections in the midbrain of the normal elephant, called attention to the importance of the fibers going to the facial nucleus, which nucleus plays a large part in the motor mechanism of the trunk. He found that two thirds of the fibers contained in the motor pathway from the cortex terminated in the facial nucleus. He called attention to the marked difference in the size of the pyramidal

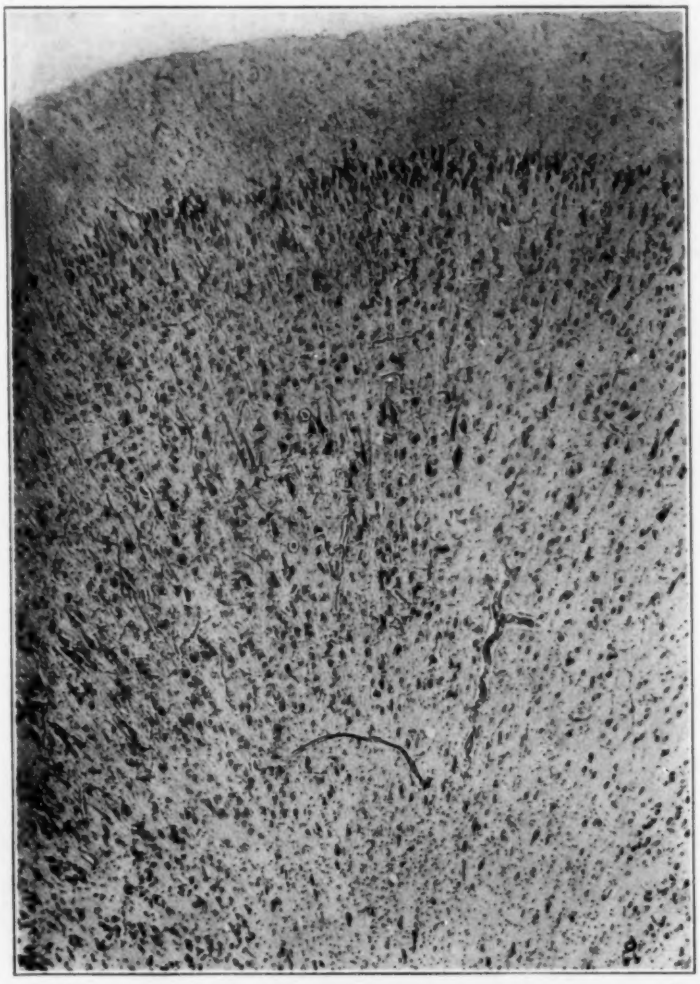


Fig. 11.—From the motor cortex at Area 4 in Figure 17. This differs from the cortex of the motor area as shown in Figure 10 in that the second layer is not so broad; the area between the second and fifth layers is broader; the fifth layer is not so rich in cells, and the individual cells are smaller; × 80.

10. Bregmann, L. E.: Neue Untersuchungen zur Kenntnis der Pyramidenbahn. 2. Die Oblongatapyramide des Elephanten, Anat. Anz. **48**:235-240, 1915-1916.

tract in a section through the anterior portion of the pons above the facial nucleus, and in another section in the caudal end of the pons after the facial fibers were given off. There was also further diminution in the pyramidal tract at the level of the olive so that he concluded some fibers were given off to the nuclei of the lower motor cranial nerves.

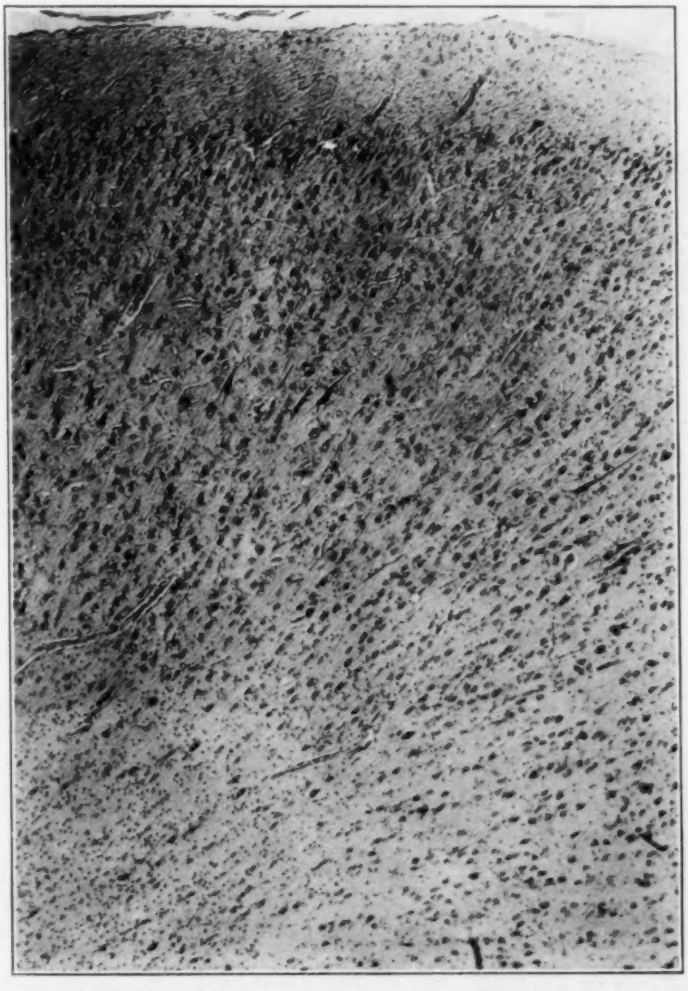


Fig. 12.—From the motor cortex at Area 5 in Figure 17. The cell structure is quite unlike that in Figure 10; × 80.

The work of Hoche,[11] in connection with two fatal cases in man in which there was softening of one cerebral hemisphere, has added

11. Hoche, A.: Beiträge zur Anatomie der Pyramidenbahn und der oberen Scheife, nebst Remerkungen über die abnormen Bündel in Pons and Medulla oblongata, Arch. f. Psychiat. **30**:103-136, 1898.

much information to our knowledge of the corticotegmental bundle in the human brain. From his work, the fibers appear to pass through the internal capsule into the base of the cerebral peduncle and into the pons region where they are detached from the main mass of the

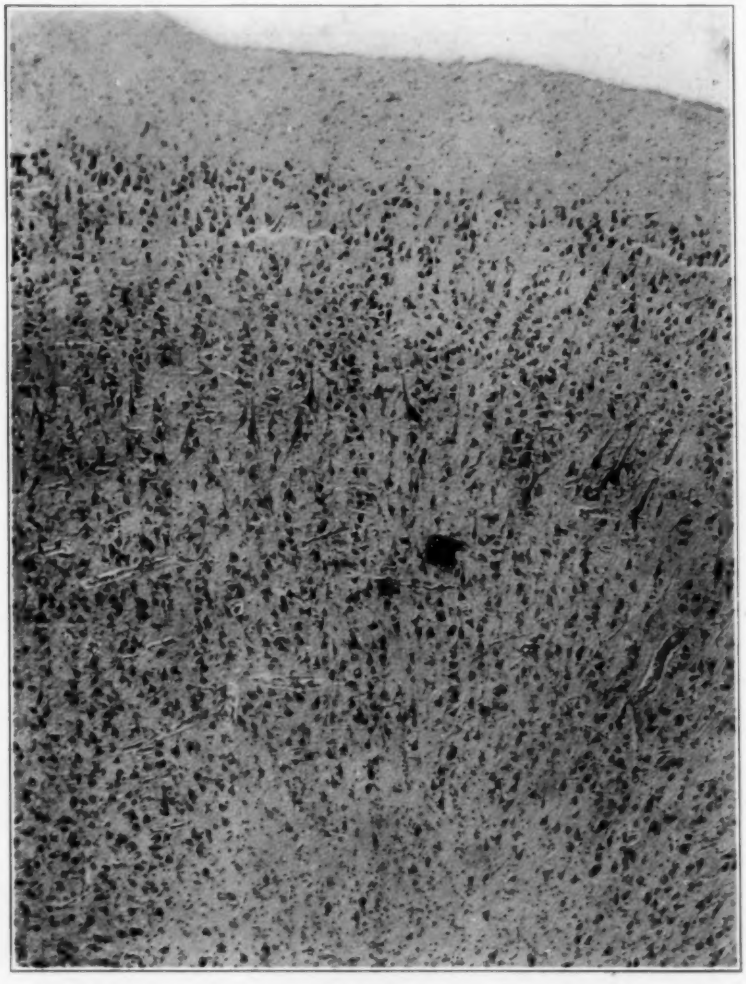


Fig. 13.—From the small gyrus at the outer extremity of the cruciate sulcus at Area 6 in Figure 17. This section resembles that of the motor cortex shown in Figure 10 in the rather broad zonal layer, the absence of a granular layer, and the presence of large pyramidal cells; × 80.

pyramidal tract and take a position in the region of the lemniscus medialis. Fibers are given off to the facial and hypoglossal nuclei of the same and opposite sides.

METHODS AND MATERIAL

The foundation of our work consisted of a complete survey of sections of the cortex, representing the cell structure, duplicated by sections representing the fiber arrangement. The cell and fiber structures were first studied in a series of frontal sections of the entire

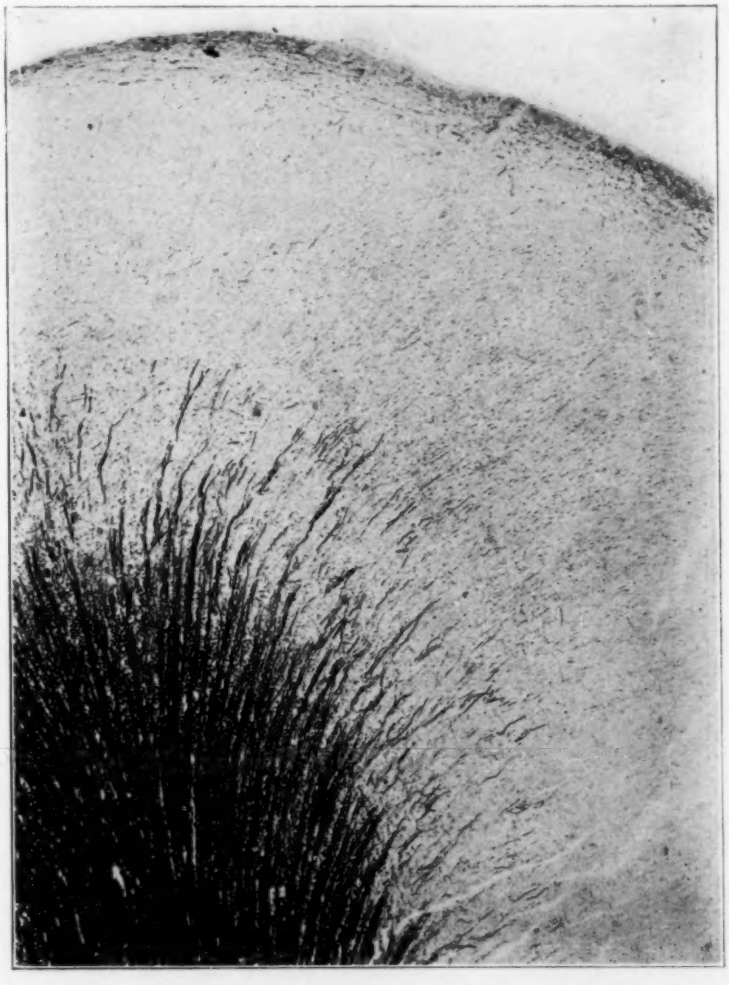


Fig. 14.—From the motor cortex at Area 2 in Figure 17. The broad layer of tangential fibers is characteristic of the cortex of the motor area; ×80.

brain; in this series the variation of the angle at which gyri were sectioned made the study of lamination very difficult. In another series the gyri were dissected individually after fixation in liquor formaldehydi and then divided into blocks, which made cutting at a right angle to the surface possible in every block. If, for example,

there was a sharp curve in the gyrus, a wedge of tissue was sacrificed so that the remaining sections were cut at a right angle to the surface. The material for cell studies was fixed in 10 per cent. liquor formaldehydi, in some instances through carotid injection. The blocks were imbedded in paraffin and sections cut at a thickness of 20 microns and

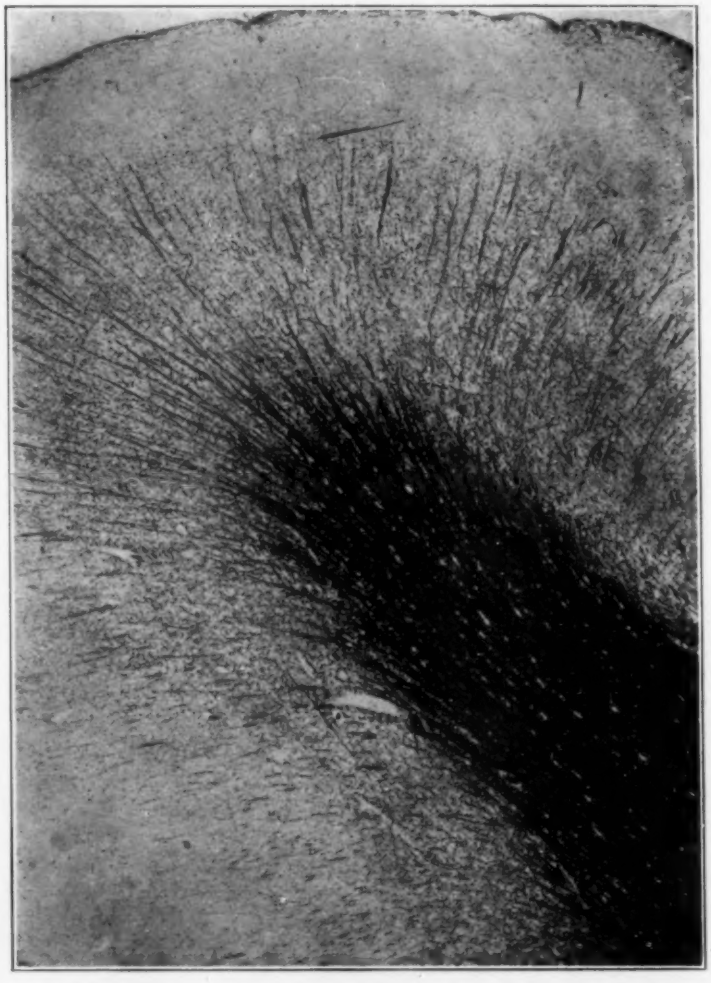


Fig. 15.—Fiber structure of the motor cortex at Area 5 in Figure 17. The narrow tangential layer of fibers may be noted; × 80.

stained with thionin. The material for fiber studies was fixed in liquor formaldehydi and mordanted in Müller's fluid for six weeks, embedded in celloidin and stained by the Weigert-Pal method, and sectioned at 20 microns. After study of these sections an effort was made to outline the motor cortex; but because the histologic arrangement was not

altogether unequivocal, a series of stimulation experiments was undertaken. Under cocain anesthesia various parts of the cortex were exposed and stimulated by the bipolar method and the findings checked by the unipolar method; the Petzold coil was used and the current registered on the centimeter scale. Thirty experiments were performed on eighteen sheep.

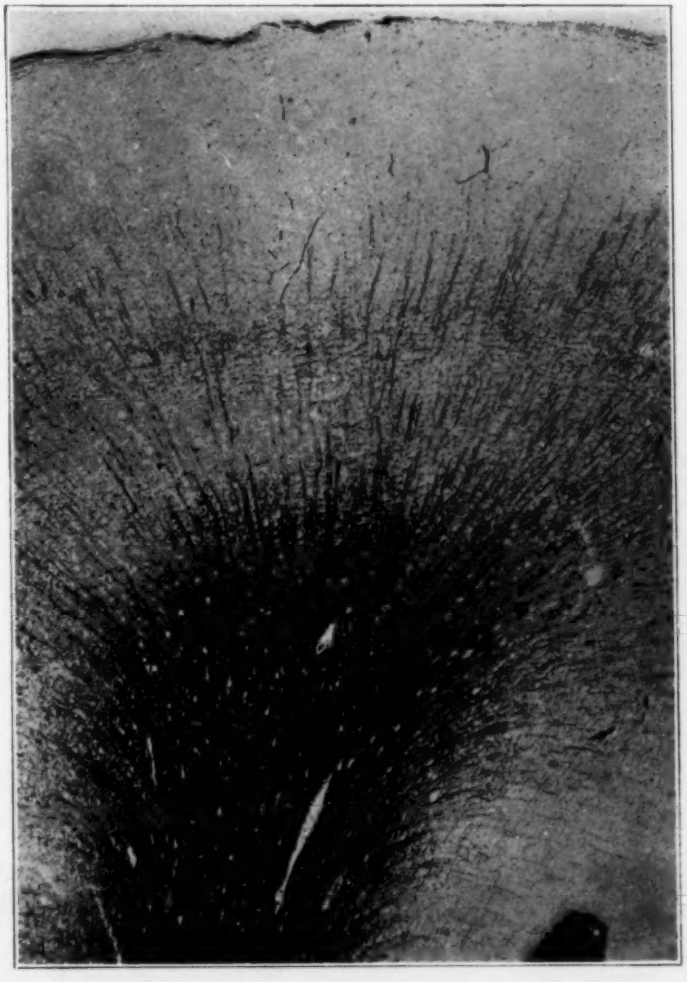


Fig. 16.—From Area 6 in Figure 17, showing the narrow tangential layer of fibers; × 80.

Extirpation of the motor cortex followed in the animal stimulated. The pia over the crest of the gyrus was divided and then gently peeled from the gyrus. This greatly reduced the danger of interfering with the circulation of the surrounding cortex or of direct injury to the

adjacent gyri (Fig. 18). After extirpation the animal was killed in from twenty-seven to thirty days. The brains were fixed in Müller's fluid through carotid injection and immersion for from ten to fourteen days. Three millimeter blocks were then cut and stained by the Marchi method, when they were embedded in celloidin.

### HISTOLOGIC STUDIES

To obtain the landmarks of the cortex the fissuration of the brain was studied in a series of fetuses; at full term the average head-rump

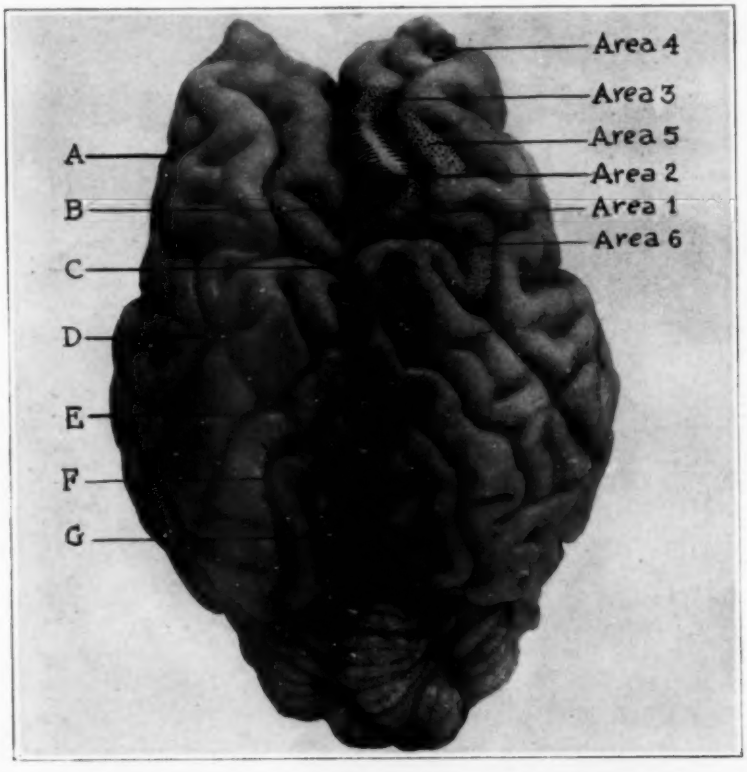



Fig. 17.—Dorsal surface of the sheep brain: Areas 1 and 2, centers for movements of the extremities; Area 3, center for movements of the head and eyes to the opposite side; Area 5, center for movements of the face muscles of the same side; Area 6, an area histologically of the motor type of cortex, but which gives no response on stimulation. *A*, sulcus diagonalis; *B*, sulcus splenialis; *C*, sulcus cruciatus; *D*, sulcus suprasylvius; *E*, sulcus lateralis; *F*, sulcus intermedius, and *G*, sulcus medialis.

measurement of the fetus was 50 cm. The hippocampal fissure appeared at a very early stage and the rhinal fissure in the 14.5-cm. embryo. In the 15.5-cm. embryo, the splenial sulcus was well marked; there was a broad depression at the site of the Sylvian fissure

and a slight, narrow, vertical depression on the anterior extremity, which was the beginning of the coronal sulcus (Fig. 7). At the appearance of this sulcus lamination had not commenced. In the brain of the 21-cm. embryo the beginning of lamination was seen very satisfactorily, while in the brain of the 24-cm. embryo, in which the coronal sulcus was already deep, the cell structure of the cortex presented definite lamination. There was found to be a very rapid progress in fissuration and lamination between this stage and that of the 30-cm. embryo (Fig. 8), in which the cell picture and the development of the coronal sulcus with its various ramifications approached that of the adult brain. The Betz cell layer of the brain of this 30-cm. embryo was particularly interesting in that it could

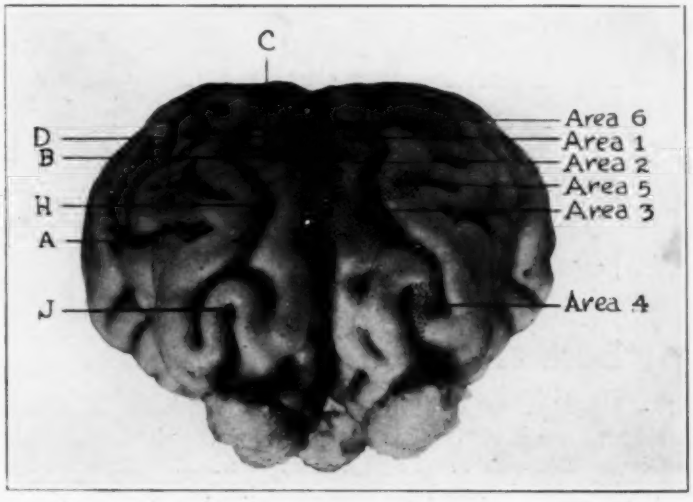



Fig. 18.—Frontal surface of the sheep brain: Areas 1, 2, 3, 5 and 6 as in Figure 17; Area 4, center for the movements of the face muscles of the opposite side: *A*, *B*, *C* and *D*, as in Figure 17; *H*, sulcus coronalis; *J*, sulcus praesylvius.

be followed from the mesial surface of the superior frontal convolution over the crest into the depth of the coronal sulcus and almost to the crest of the "middle frontal" convolution, where it abruptly changed to a layer of small, thinly scattered cells (Fig. 9).

On the basis of cell types and lamination, eight distinct cortical areas were outlined in each hemisphere of the adult sheep brain; one of these areas, located on the superior frontal convolution, was designated as the motor cortex. Its chief characteristics were a broad first layer, a very rich second layer, a poor third layer, absence of the granular layer, while the fourth layer contained numerous large pyramidal cells which were slightly larger than the pyramidal cells

of this layer found in other parts of the cortex and present in a much larger number. The fifth layer presented nothing distinctive (Fig. 10). Toward the extreme anterior portion of the superior frontal convolution the cells of the fourth layer were less prominent. The cell structure of the superior frontal convolution has been well described by King,[12] who concluded that it is characterized by elements analogous to those of the motor cortex of man. The portion of cortex bounded laterally by the outer prolongation of the coronal sulcus and mesially by the presylvian fissure (Fig. 14, Area 4) histologically presented some of the characteristics of the cortex of the superior frontal convolution in that there was a broad zonal layer, a narrow, though closely packed, second layer and prominent fourth layer (Fig. 11).

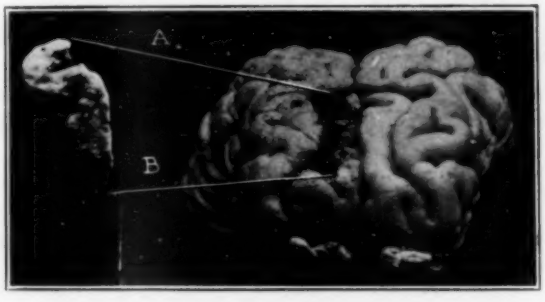



Fig. 19.—Frontal view of sheep brain from which the superior frontal gyrus has been extirpated between *A*, posteriorly, and *B*, anteriorly. The absence of injury to the surrounding gyri may be noted. The insert shows the superior frontal gyrus as removed intact from the brain.

The cortex of the "middle frontal" convolution differed from that of the superior frontal convolution in that the zonal layer was not so wide; the cells of the second layer were more loosely placed, while those of the fourth layer were much smaller in size and fewer in number (Fig. 12). On the mesial surface of this gyrus, however, the structure was very much like that of the superior frontal convolution. Adjacent to the posterior portion of the motor area, at the outer extremity of the cruciate sulcus, there was a small U-shaped gyrus, the fourth layer of which contained a few pyramidal cells which were larger than the pyramidal cells in the fourth layer of the superior frontal convolution (Fig. 13).

12. King, J. L.: Localization of the Motor Area in the Sheep's Brain by the Histological Method, J. Comp. Neurol. **21**:311-320, 1911.

Fig. 20.—Degeneration in the crus after extirpation of Area 5 in Figure 17; the prolongation backward of the degenerated fibers *A* may be noted; these fibers later become isolated as the corticotegmental bundle; ×8: *C*, tegmentum; *D*, bracchium conjunctivum positcum; *E*, central gray; *F*, superior colliculus; *G*, tractus peduncularis transversus; *H*, cerebral peduncle; *J*, ganglion interpedunculare; *K*, root of oculomotor nerve; *L*, nucleus ruber; *M*, substantia nigra; *N*, posterior longitudinal bundle; *O*, oculomotor nucleus; *P*, thalamo-olivary bundle; *Q*, raphé; *R*, mesencephalic root of trigeminal nerve; *S*, midbrain ventricle; *T*, stratum medullare profundum; *U*, stratum medullare intermedium; *V*, stratum medullare superficiale, and *W*, stratum zonale.

The fiber structure of the superior frontal convolution differed from that of the surrounding cortex in that the tangential layer was much broader (Fig. 14). The tangential layer of the middle frontal convolution (Fig. 15), as well as that of the gyrus surrounding the outer end of the cruciate sulcus (Fig. 16), in which the large pyramidal cells were found, was very shallow.

### STIMULATION EXPERIMENTS

As a result of the stimulation experiments we were able to outline five excitable areas (Figs. 17 and 18). Area 1 was located at the

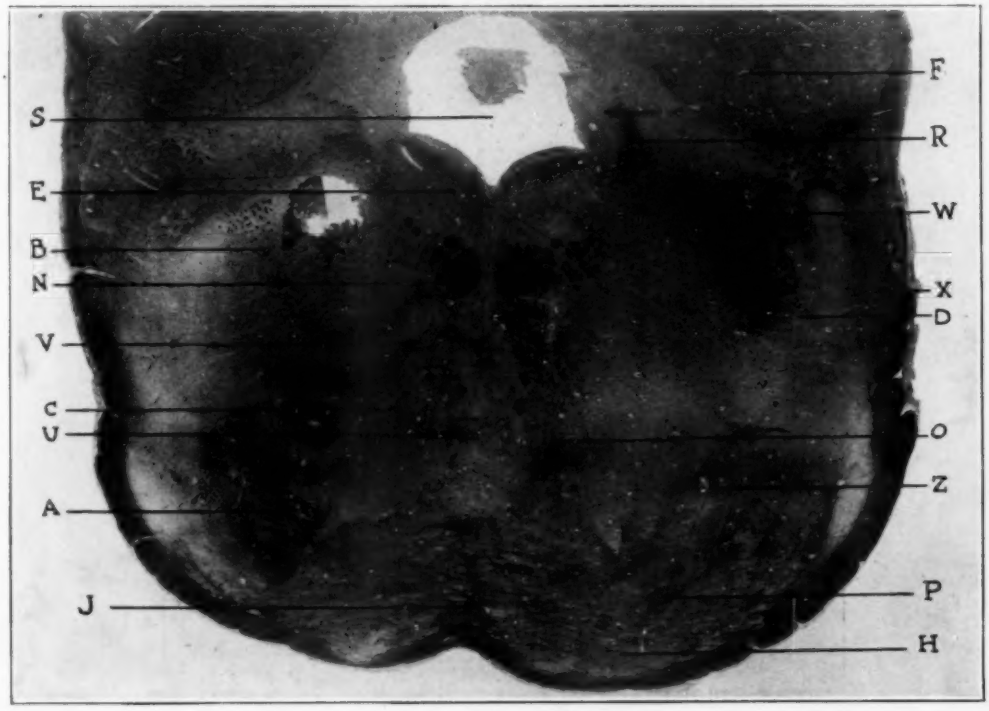



Fig. 21.—*A*, degeneration in pyramidal tract; *B*, isolated degeneration of corticotegmental bundle; *C*, reticular formation of tegmentum; *D*, superior cerebellar arm; *E*, central gray; *F*, inferior colliculus; *H*, pons; *J*, ganglion interpedunculare; *N*, posterior longitudinal tract; *O*, colliculospinal tract; *P*, corticospinal fibers; *R*, mesencephalic root of trigeminal nerve; *S*, midbrain ventricle; *U*, Forel's decussation; *V*, nucleus of Gudden; *W*, central tegmental bundle; *X*, lateral fillet, and *Z*, mesial fillet; ×8.

posterior extremity of the superior frontal gyrus between the cruciate sulcus and the indentation of the splenial sulcus. Area 2 extended from the indentation of the splenial sulcus forward for about 8 mm. Area 3, about 8 mm. in length, was in front of Area 2. Areas 2 and

3 were sometimes separated by a small area of nonexcitable cortex; but in other experiments they were found to be continuous and in still others they were found to overlap. The anterior extremity of Area 3 never extended to the extreme anterior portion of the gyrus. Area

Fig. 22.—Photomicrograph showing the density of the degeneration at *A* in Figure 21; × 125.

4 was located in the narrow convolution between the outer anterior spur of the coronal sulcus and the frontal end of the presylvian fissure. Area 5 was located in the portion of the middle frontal gyrus adjacent to the coronal sulcus. In most of the experiments this area was found

to be about 1 cm. square and located opposite the midportion of the coronal sulcus; but in some of the experiments it was found to be slightly more anteriorly placed. These five excitable areas are indicated in Figures 17 and 18; and, in addition, there is indicated a sixth area, which though not responding to electrical stimulation, is of sufficient

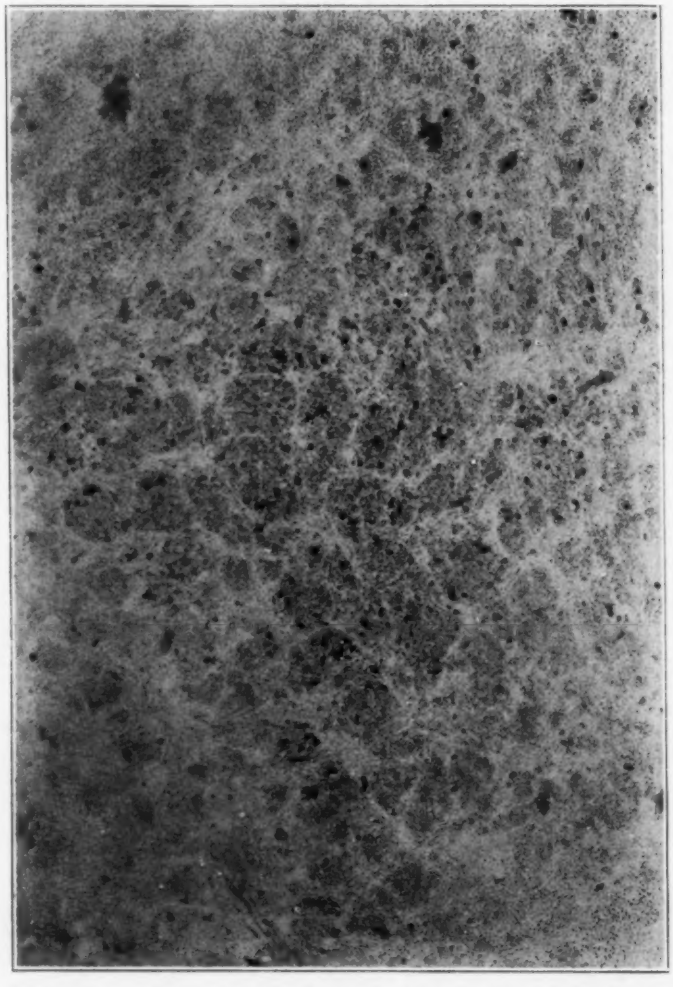


Fig. 23.—Photomicrograph showing the degeneration at *B* in Figure 21; ×125.

importance because of its architecture to be included in this study. Hereafter, I shall refer to areas from 1 to 6 without reference to Figures 17 and 18.

Stimulation of Areas 1 and 2 gave reactions in the extremities and occasionally in the trunk. Repeated efforts were made in both

hemispheres to determine the individual areas for the four extremities; with very few exceptions the reaction occurred in more than one limb and, unless the current was kept at the minimum, a reaction occurred in all four extremities. When the current was reduced sufficiently so that only one or two limbs responded, although we can state no definite rule as to contralateral or ipsilateral reactions, since both occurred with almost equal frequency, we obtained many times movements of the opposite hind limb and the fore limb of the same side. Because of this association in the movements of the hind limb of one side and the fore limb of the other side, an attempt was made to

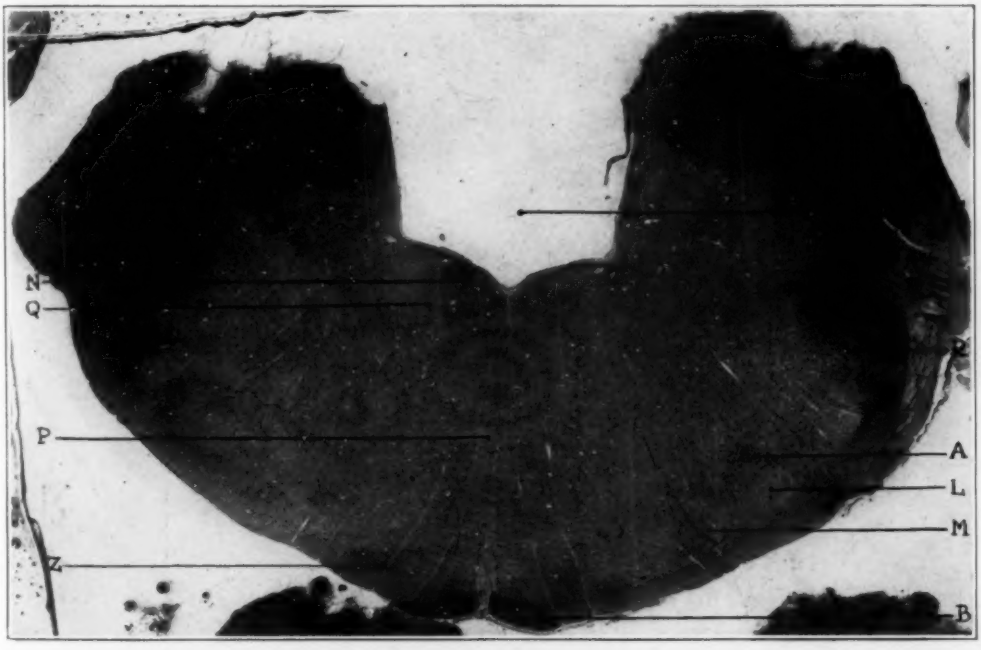



Fig. 24.—Marking the caudal end of the degeneration of the corticotegmental tract *A* at the position of the facial nucleus: *B*, pyramidal tract; *L*, facial nucleus; *M*, superior olive; *N*, posterior longitudinal bundle; *P*, colliculospinal bundle; *Q*, abducens nucleus; *R*, spinal root of trigeminal nerve; *S*, hind brain ventricle, and *Z*, mesial fillet; ×8.

determine the character of the movements as concerned progression. In most cases, however, the movements consisted of contraction of muscles of a single group, so that typical progressive movements could not be brought out. One can, however, say with certainty that the movement of two or more limbs did not occur with definite rhythm. In summing up all of the experiments on Area 1 there was a greater number of reactions in the hind legs and a greater number in the hind leg of the opposite side. In Area 2 there was a greater number

of reactions in the fore limbs and the reactions of the limb of the opposite side were slightly greater. In addition to the limb movements, some movements of the trunk were observed but these were not conspicuous. In some experiments, Areas 1 and 2 gave movements of the head and eyes to the opposite side, but this was certainly the exception.

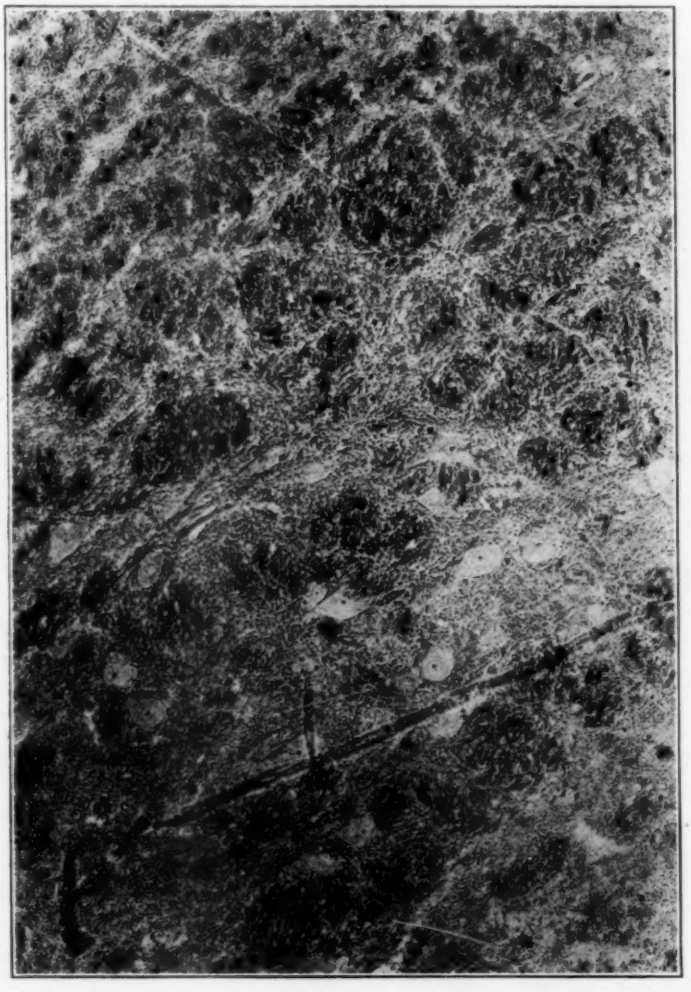


Fig. 25.—Photomicrograph taken from *A* in Figure 24, showing large cells of the facial nucleus among which are degenerated fibers of the corticotegmental bundle; × 125.

In Area 3 the movements of the head and eyes to the opposite side were always easily demonstrated and with few exceptions were the only reactions which occurred after stimulation of this area.

Stimulation of Area 4 produced contractions of the muscles of the opposite side of the face and the contractions were usually more marked in the lower lip. This result was usually easily obtained and with less current than was required to bring about reactions in the limbs in Areas 1 and 2; in some experiments, however, it was difficult to bring out, and in these animals it was also impossible to get the characteristic contractions of the opposite face muscles in any of the surrounding cortex. The reaction following stimulation of this area, however, was in the contralateral face muscles only, unless the current

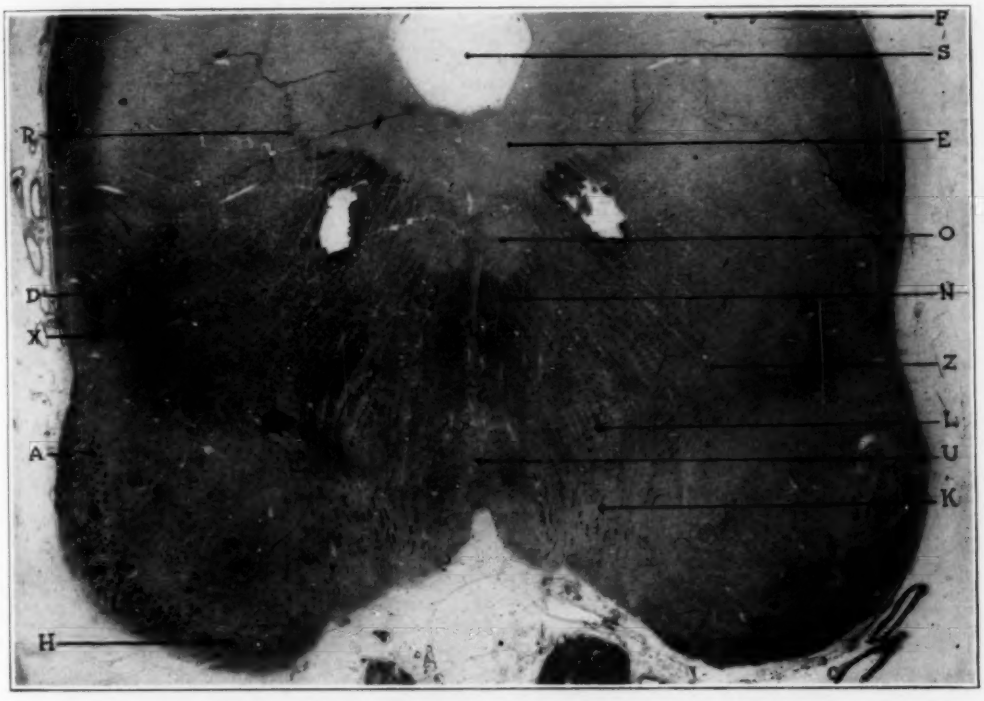



Fig. 26.—Degeneration in the crus after extirpation of Area 6. The very slight degeneration *A* extending toward the tegmentum, and its extreme lateral position as compared with the degeneration in Figure 20 may be noted: *D*, bracchium posticum; *E*, central gray; *F*, superior colliculus; *H*, cerebral peduncle; *K*, oculomotor nerve; *L*, nucleus ruber; *N*, posterior longitudinal bundle; *O*, oculomotor nucleus; *R*, mesencephalic root of trigeminal nerve; *S*, midbrain ventricle; *U*, Forel's decussation; *X*, superior mesial fillet, and *Z*, mesial fillet; ×8.

was sufficiently strong to spread to the ipsolateral face area (Area 5) across the coronal sulcus.

Stimulation of Area 5 gave ipsolateral contractions of the face muscles and the reactions were usually more marked in the upper lip. This result was constantly obtained in this area and characteristic

reactions were in almost every case produced with a current less strong than that necessary to produce reactions in the other areas.

During the course of the experiments the entire dorsal and lateral surfaces of both cerebral hemispheres were repeatedly stimulated without noticeable muscle contractions in the periphery. The portions of the cortex just posterior to the cruciate sulcus and that surrounding the outer extremity of this sulcus were very carefully searched for even small points of excitability, but always without positive results. One special experiment was performed in an effort to determine the

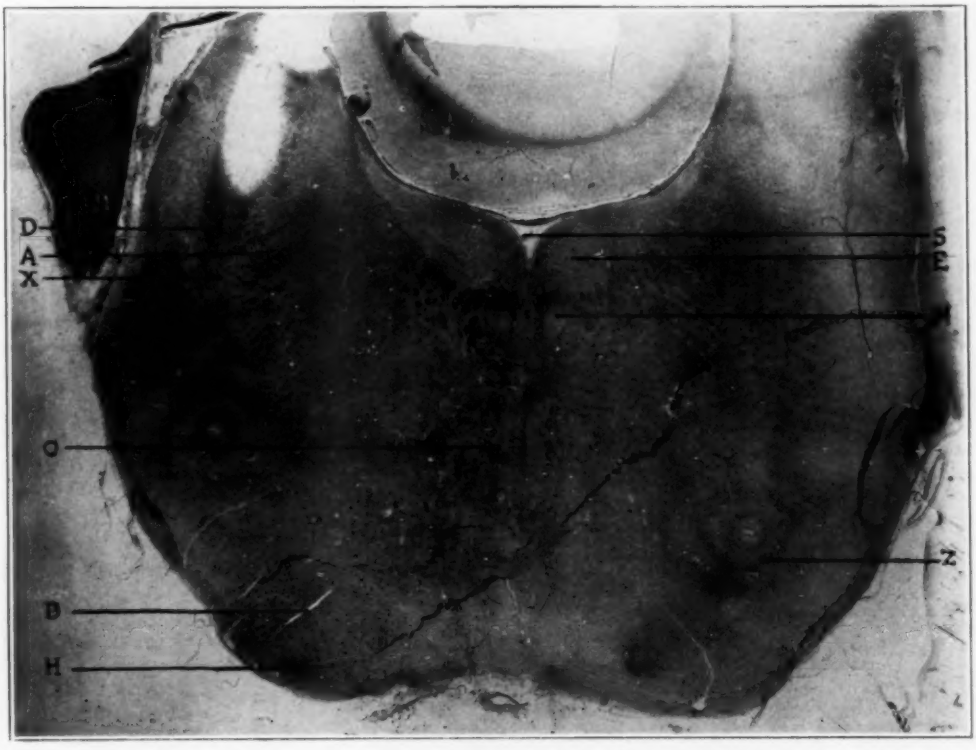



Fig. 27.—Caudal end of the cortico-tegmental tract degeneration *A*, after extirpation of Area 6; *B*, degeneration in pyramid; *D*, superior cerebellar arm; *E*, central gray; *H*, peduncle; *N*, posterior longitudinal bundle; *O*, colliculospinal bundle; *S*, ventricle; *X*, lateral fillet, and *Z*, mesial fillet; ×8.

excitability of the gyrus (Area 6) surrounding the outer extremity of the cruciate sulcus. In this animal the five excitable areas responded to a current ranging from twelve to ten; but there was no response in this cortex (Area 6) at a current of eight, beyond which it was useless to go because of the probability of spread. In this animal the gyrus was extirpated and a very definite pyramidal tract degeneration was demonstrated in Marchi preparations (Fig. 28).

The variation in the conclusions of previous workers is evidence of the difficulty encountered in attempting to establish definite areas of excitable cortex in the sheep brain. Our conclusions, which led to the outlining of five excitable areas, as indicated in Figures 17 and 18, were possible only after frequently repeated attempts. With a view to avoiding the possibility of misinterpretation some of the protocols are given below. Areas 1 to 5 indicate the areas as shown in Figures 17 and 18. The numerals before each result indicate the position of the coil on the centimeter scale of the Petzold apparatus,

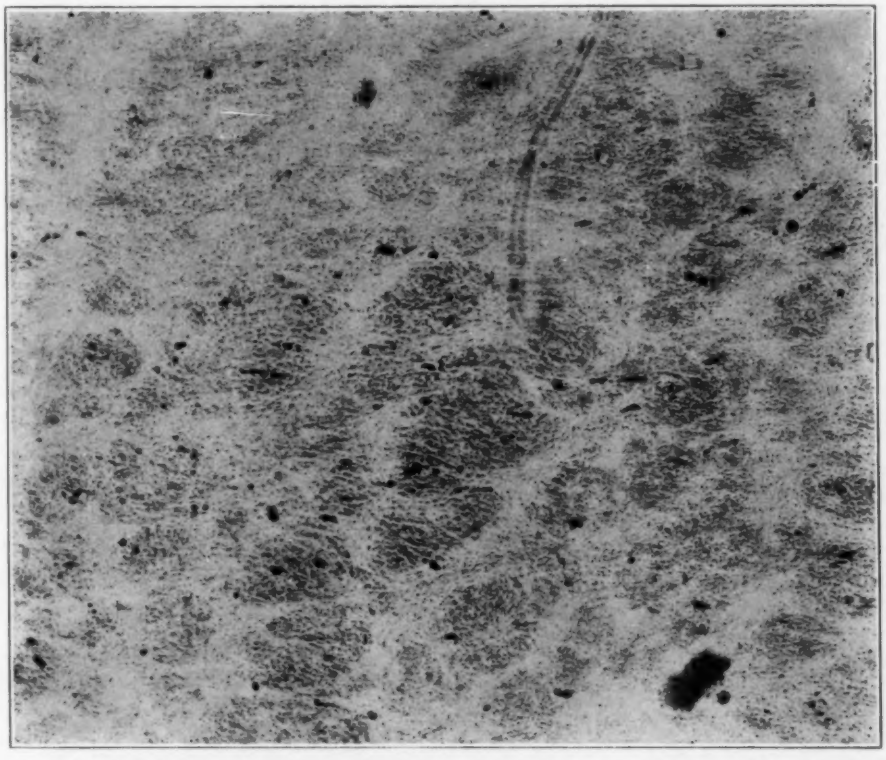


Fig. 28.—Photomicrograph showing the slight evidence of degeneration in the corticotegmental bundle after extirpation of Area 6, taken from *A* in Figure 27; × 125.

at which the reading was made. The stimulations were always commenced with a very weak current and a record made at a point where the current was sufficiently strong to cause a reaction. As will be found in the protocols, an effort was always made to determine the weakest current at which a given reaction could be obtained. In some experiments all areas of both hemispheres were stimulated; in others all areas of one hemisphere, while some experiments were devoted to the consideration of a limited number of areas of the cortex of one hemisphere.

TABLE 1.—Results of Experiment 4 *

Right Hemisphere

| Area 1 | Area 2 | Area 3 | Area 5 |
|---|---|---|---|
| 12.5—R.F., L.H. and L.F., slight movement; all lifting and toe spreading | 12.5—L.F., slight movement; R.H. and R.F., constant on repeated trial | 12—R.F. and L.F., forward; R.H., back and upward (delayed); L.H., back and upward (delayed) | 11.5—Both lips to right, lower more markedly |
| 12—L.H., R.F. and L.F., delayed; all three with toe spreading | 12—R.H., L.H. and R.F., slight; L.F., very slight | 11.5—Head pulls to left; R.F., strong; R.H. and L.F., slight<br>11.5—R.F. and L.F., forward; R.H., back and upward (delayed); L.H., back and upward (delayed) | 10—Upper lip puckered, indefinite<br>10—Right upper lip elevated<br>10—Nose and upper lip to right |
| | 11.5—R.H., pulled forward; R.F., pulled forward; L.F., one half as much as R.F.; L.H., very slight | 10—L.H., extension followed by flexion; L.F., extension forward; R.F., forward, but slighter | |

Left Hemisphere

| | | | |
|---|---|---|---|
| 10—R.H., slight extension; L.F., extension, more slight | 10.5—Head pulls back to right | 11—Head to right; R.H., up; R.F., up and forward; stronger current brings in both sides | |
| 9.5—R.H. and L.F., slight extension | 10—Head pulls back to right; R.H. and L.F., up; R.F., up slightly<br>10—R.H., forward; R.F., forward (delayed); L.F., very slight | 10—R.H., up; R.F., up and forward | |
| | 9.5—Head pulls back; L.H., forward; R.H., forward stronger; R.F., forward<br>9.5—L.F. and R.H., forward; L.H. and R.F., delayed | 9.5—Head rotates to right strongly; R.F., back and outward | |
| | 9—Head pulls back; R.H., R.F. and L.F., forward<br>—R.H., forward and up; L.F., backward<br>—R.H., L.H. and R.F., forward and up; L.F., backward | 9—Head rotates to right strongly; R.F., back and outward | |

* In this and the following table, R.F. indicates right fore leg; R.H., right hind leg; L.F., left fore leg, and L.H., left hind leg.

TABLE 2.—Results of Experiments 11, 12, 13, 14, 15 *

Right Hemisphere

| Area 1 | Area 2 | Area 3 | Area 4 | Area 5 |
|---|---|---|---|---|
| 9.5—Outer extremity of the area: L.F., slight flexion | 9.5—Outer extremity of the area: L.H., adduction slighter than right; R.H., adduction; L.F., flexion, slighter than in Area 1; R.F., toe spreading, definite slow turning movements of head and eyes to left (found only on the surface of the area) | 10—Same as in Area 2 except that movements are more pronounced; tail wiggles, spasms of face muscles, chewing motion again brought out at this point, apparently due to long continued stimulation; definite head and eyes to left | 9.5—Firm contraction of left face muscles with rotation of head to left | 10—Usual homolateral face movements |
| 10—No response | 10—R.H., pulling outward and backward, distinct, very marked; L.F., stiffening and pulling backward, very slight; R.F., toe spreading, very slight; pulling backward of head and eyes to left<br>10—Definite, head and eyes to left | 10.5—L.H., flexion; L.F., strong extension and toe spreading; R.F., slight extension of knee with toe spreading, followed by marked flexion of knee and shoulder; tail wiggles; also grinding of mouth; head and eye movements to left; quick spasm of right face muscles | 9, 9.5, 10, 10.5—No response | 11—More definite movement of upper lip with some pulling of nostril to right |
| 11—Outer extremity of area: drawing back of head<br>11.—L.F., flexion at knee and shoulder; lifting and pawing; inner extremity of the area; L.H., raising or pulling up | 11—R.H., pulling outward and backward; drawing back of head (more pronounced than in Area 1); drawing of head to left, without eye movements<br>11—L.H., slight adduction; R.H., slightly raised and pulled forward; L.F., abducted forward; R.F., slight adduction and stiffening<br>11—L.H., forward slightly abducted; R.F., definite slight abduction | 11—Definite drawing of head and eyes to left | 10—Head and eyes to left (head and eye movements seem to extend over what is ordinarily Areas 3 and 4, about 14 mm.) | 12—Slight definite contraction of muscles of upper lip on both sides |
| 12—Outer extremity of the area: L.F., flexion at knee and shoulder; lifting and pawing | 12—L.H., slight adduction; R.H., slightly raised and pulled forward; R.F., slight abduction and stiffening; L.F., forward and slightly abducted; R.H., pulled forward; R.F., definite slight abduction<br>12—L.F., occasional extension (followed by facial spasm, a violent struggling motion without chewing); head and eyes to left<br>12.25—R.H., very slight abduction; R.F., very slight pulling forward | 9.5—Head and eyes to left | 10.5—Definite contraction of muscles of left side of face with only very slight pulling of head to left | |

* These five experiments were performed on one animal, which gave results somewhat at variance with our other results, illustrating what is believed to be a marked individual variation in the reaction of the cortex.

TABLE 2.—Results of Experiments 11, 12, 13, 14, 15 (*Continued*)

Left Hemisphere

| | | | | |
|---|---|---|---|---|
| 8.5—L.H., pulling out and forward; R.H., raising; L.F., toe spreading; R.F., raising | 7.5—On the dorsal surface at the mesial side of the area: pulling of head and eyes to right; on the lateral surface of the area: L.H., pulling forward, less active than R.H.; L.F., late toe spreading and extension of toes; R.F., toe spreading after flexion, stronger than L.F. | 7.5, 8.5—L.H., pulling out and slightly forward; L.F., late toe spreading and extension of toes; R.H., stepping downward; R.F., turning downward and forward of hoofs; movement of whole pelvis to right | 9—Rotation of head with elevation of nose, with slight contraction of right face, followed by strong contraction of left face | 9.5—Elevation of angle of left upper lip and left lower lip |
| 8, 9, 9.5, 10, 10.5, 11.5, 12—No response | 8.5—L.H., lifting upward; R.H., extension; L.F., slight extension; R.F., flexion and extension | 9, 9.5—No response | 10.5—Quick response with grinding of teeth and pulling of jaw to left; definite rotation of head with marked contraction of face muscles of opposite side | 10—Homolateral face (followed by active chewing and muscle spasms on both sides, so further stimulation was impossible) |
| 12.25—On the outer extremity of the area: L.H., abduction and flexion of the whole limb markedly; R.F., pulling up of entire limb (repeated several times); on the inner extremity of the area: no response | 9—Very quick response of head and eyes to right | 10—Head and eyes to right | 9, 9.5, 10.5—Rotation of head with elevation of nose to right without contraction of face muscles | 10.5—Homolateral face |
| 14.—L.H., same as at 12.25, but very slightly; R.F., same, but diminished | 9.5—Very quick response of head and eyes to right | 10.5—Pulling of pelvis to right, shoulder to left; no leg movements | 10—Chewing motion with quick contraction of left lower lip; also contraction of muscles at both sides of nose | 11.5—Stimulation of Areas 4 and 5 caused violent contraction of both sides of face indicating spread from homolateral to contralateral face area and vice versa |
| 14.5, 15, 15.5, 16, 16.5—Same response as with stronger current | 10—Head and eyes to right; R.H., slight forward movement; R.F., slight pulling forward | 11, 11.5—No response | 11.5—Stimulation of Areas 4 and 5 caused violent contraction of both sides of face, indicating spread from homolateral to contralateral area and vice versa | 10, 10.5—Elevation of angle of left upper lip |
| | 10, 10.5—L.H., mild pulling up; R.H., extension and pulling forward; R.F., slight abduction and toe spreading; head and eyes to right sharply | 11.5—Head and eyes to right | 11, 12—No response | 11, 10.5, 9.5, 9, 12—No response |
| | 11.5—On the dorsal surface at the mesial surface of the area: head and eyes to right | 12—Head and eyes to right<br>12—No response | | |
| | 12—Definite slow movement of head and eyes to right; on the dorsal surface on the mesial side; no response | | | |
| | 11—On the dorsal surface at the mesial side of the area: head and eyes to right | | | |

TABLE 3.—Results of Experiments 16 and 17

Right Hemisphere

| Area 1 | Area 2 | Area 3 | Area 4 | Area 5 |
|---|---|---|---|---|
| 9—L.F., constant flexion is not obtained | 9—R.H., pushing backward; L.F., sharp pulling up; R.F., adduction; when repeated, only L.F. sharp raising | 10—Head and eyes to left | 9—Strong contraction of muscles of face on the left side | 9—Strong contraction of muscles of right face |
| 10.5—On the outer extremity of the area: L.F., flexion is not constant | 10—L.F., pulled forward actively; R.F., pulled forward slightly; R.H., pulled forward (in the anterior portion of this area there is definite trunk movement with extension of L.F.) | 11—Head and eyes to left | 10.—Contraction of muscles of left side of face | 10—Contraction of muscles of right face |
| | | 11.5—No response | | |

Left Hemisphere

| | | | | |
|---|---|---|---|---|
| 9.5—No response | 10—Same as at 10.5, but not constant | 10—Head and eyes to right | 10—Strong contraction of muscles of right side of face | 10—Contraction of muscles of left side of face |
| | 10.5—Toward the mesial aspect of the area: L.H., lifting and moving slightly forward; L.F., slight extension forward; R.F., slight extension forward, less in extent; all responses not constant | | | |
| | 10.5—Toward the outer side of the area: R.F., brisk lifting | | | |
| | 9.5—L.H., slight abduction; L.F., slight pulling forward; R.F., brisk lifting | | | |

TABLE 4.—Results of Experiment 23

Right Hemisphere

| Area 1 | Area 2 | Area 3 | Area 4 | Area 5 |
|---|---|---|---|---|
| 10.5—L.F., abduction and flexion; stronger current brings out movements of all four legs, particularly L.F. | 10.5—Strong current brings out movements of all four legs, particularly L.F.; R.F., slight knee lifting | 10—Head and eyes to left | 9—Characteristic face reaction, chiefly of lower lip of opposite sides | 10—Contraction of muscles of right face about 1 cm. further along coronal sulcus than usually found |
| 11.—L.F., abduction and flexion; R.F., slight, which comes in late with slight flexion; stronger current brings out movements of all four legs, particularly L.F. | 11—Stronger current brings out movements of all four legs, particularly L.F. | 10.5—Head and eyes to left | 10—Contralateral face reaction | 10.5—Contraction of muscles of right face about 1 cm. further forward along coronal sulcus than usually found |
| | 13—L.F., toe spreading and slight abduction; L.H., toe spreading and pulling forward; R.F., slight knee raising | | | |

TABLE 5.—RESULTS OF EXPERIMENT 30

**Right Hemisphere**

| Area 1 | Area 2 | Area 3 | Area 4 | Area 5 |
|---|---|---|---|---|
| (Not tested) | (Not tested) | 11.5—Head and eyes to left | 12—Definite puckering movements of both right and left sides (more marked on right) involving both upper and lower lips; if stimulation is continued there is licking of lips with tongue | 11—More marked reaction, same as at 12; fibrillary twitching occurs when contact is slightly prolonged |
| | | | | 10—Definite chewing movements not defensive, but ceasing with removal of electrode; no saliva flow; repeatedly obtained in right hemisphere |
| | | | 13—Definite right upper lip | 12—Slight quick movement of right upper lip, elevation coinciding exactly with contact of electrode |
| | | | | 13—Definite right upper lip, which is obtained only at knee of sulcus |

**Left Hemisphere**

| | | | | |
|---|---|---|---|---|
| 11.5—R.H., predominating; L.H., and L.F., slight; R.H. and R.F., slight when repeated | 11.5—L.H., predominating; R.H., comes in with L.F.; L.H., alone when repeated † | 12.5—Head and eyes to left | 10—Very definite contralateral twitching of lower and upper lips, chiefly lower | 13—Definite retraction and elevation of left upper lip (at knee of sulcus for a very limited area) |
| | | | 11.5—Very active upper lip and fairly well marked lower lip on both sides, right stronger | |
| | | | 13—No response; this includes everything of both sides of sulcus one | |

† Cortex just posterior to cruciate sulcus gave no response. Small U shaped gyrus surrounding outer extremity of cruciate, no response.

EXTIRPATION EXPERIMENTS

In the extirpation experiments, stimulation Areas 1, 2 and 3, as previously described, were extirpated en masse. Stimulation Areas 4 and 5 were extirpated separately. The small U-shaped gyrus surrounding the outer extremity of the cruciate sulcus (Area 6), which contained very large pyramidal cells but gave no reactions when stimulated, was also extirpated separately. In the Marchi sections, after extirpation of all of these areas, a degeneration could be followed through the corona radiata, into the internal capsule, the peduncle, the pyramidal tract and after decussation, to the upper cervical segments of the spinal cord. In addition there was always a degeneration shown by very much smaller dots extending through the corpus callosum and in almost all instances to the same gyri of the opposite side.

The study of the main mass of the pyramidal tract after extirpation of various areas of the cortex revealed findings similar to those previously described by Dexler and Margulies [5] and by King.[6] Examination of the Marchi preparations of frontal sections made at a high level of the crus revealed variations in the position of the degenerated fibers in the crus following extirpation of the different areas.

After extirpation of stimulation Areas 1, 2 and 3 in the superior frontal gyrus, the degeneration involved chiefly the middle portion of the pes, there being no degeneration dots in the most mesial and most lateral bundles. The dots were very numerous, rather compact and varied in size from very minute to rather large ones. After extirpation of stimulation Area 4, the degeneration was very generally scattered over the structure, involving all except a very small area on the mesial side and a little larger area on the lateral side. The dots were much fewer in number and smaller than those observed in sections after extirpation of Areas 1, 2 and 3. After extirpation of stimulation Area 5 in the middle frontal gyrus, the degeneration involved chiefly the mesial portion of the pes, there being no dots in the position of the outermost fibers of the structure. There were practically no dots in the area as large as those seen after extirpation of the superior frontal gyrus, so that when the dots were compared they ranged from small to medium size and were widely scattered. After extirpation of the small U-shaped gyrus surrounding the outer end of the cruciate sulcus (Area 6), the preparations showed rather small dots scattered chiefly through the central portion of the pes, extending toward, but not involving, the extreme lateral bundles and entirely missing the mesial bundles.

In frontal sections made at the level of the nucleus ruber, there was evidence, after extirpation of the various areas, of degenerated fibers migrating dorsalward from the peduncle into the tegmentum (Fig. 19). Ater extirpation of stimulation Areas 1, 2, 3 and stimula-

tion Areas 4 and 5, there was very little difference in the amount of degeneration extending into the tegmentum, so that Figure 20, made after extirpation of stimulation Area 5 in Figures 17 and 18, is a good representation of this degeneration after extirpation of the three areas. In the sections slightly more caudal than those just described, the degenerated tegmental fibers are separated from the main mass of the pyramidal tract, forming an almost circular area as shown diagramatically at *B* in Figure 21 and microscopically in Figure 23. These figures were made after extirpation of Areas 1, 2 and 3; but they also represent the appearance of the tegmental bundle degeneration after extirpation of Areas 4 and 5. The degenerated dots are more numerous, larger and more closely compact in the main mass (Fig. 22) of the pyramidal tract than in the tegmental bundle mass (Fig. 23). The tegmental bundle degeneration is easily followed until the section at the level of the facial nucleus is reached (Fig. 24), while beyond this point it cannot be demonstrated. At this level the degenerated fibers can be found among and surrounding the cells of the facial nucleus (Fig. 25).

After extirpation of Area 6 in the section at the level of the nucleus ruber, the tegmental degeneration was very slight and the fibers were seen in a much more lateral position (Fig. 26). The degeneration does not extend to so low a level in the brain stem as it does after extirpation of the other areas, and was last visible in the sections represented by Figure 27, a microscopic picture of which is shown in Figure 28.

## CONCLUSIONS

1. The coronal sulcus is one of the first fissures to appear in the development of the neopallium in the sheep embryo. Lamination of the cortex mesial and lateral to the coronal sulcus is well marked at a stage of development when the coronal sulcus has all the characteristics of the sulcus of the adult sheep brain. At this stage the layer of large pyramidal cells extends throughout the "superior frontal convolution" and through the mesial portion, but does not reach the crest of the "middle frontal" convolution.

2. Our histologic findings in the superior frontal convolution are the same as those described by King; and in addition the cortex of the "middle frontal" convolution and that surrounding the outer extremity of the cruciate sulcus also present somewhat the same appearance.

3. Stimulation of the posterior portion of the superior frontal gyrus produces contractions of the extremities. The cortex of the gyrus immediately in front of this area when stimulated causes movements of the head and eyes to the opposite side. Stimulation of the most anterior portion of the superior frontal gyrus gives no reaction.

Stimulation of the small gyrus (Area 4) lying between the frontal end of the presylvian fissure and the outer anterior spur of the coronal sulcus causes contraction of the *face muscles of the opposite side,* more particularly of the lower lip.

Stimulation of the "middle frontal" gyrus over an area about 1 cm. square usually opposite the middle portion of the coronal sulcus, but sometimes slightly more anterior, causes contraction of the *muscles of the face of the same side.* This center is easily excited, usually requiring less current than is necessary in the other areas.

Stimulation of the gyrus surrounding the outer extremity of the cruciate sulcus produces no reaction, notwithstanding its "motor" pattern.

There is no response to stimulation of areas posterior to the cruciate sulcus.

4. After extirpation of the excitable areas of the cortex, we agree with previous workers that there is no disturbance of locomotion. We further agree with the findings of other workers concerning the course of the main mass of the pyramidal tract, its decussation in the hind-brain, and disappearance in the upper cervical segments of the spinal cord.

In addition to the main mass of pyramidal tract degeneration, there is, however, in the tegmentum, evidence of the degeneration of a bundle of fibers. This degeneration, ipsolateral in its entire course, is first noticed in frontal sections at the level of the nucleus ruber, where the degeneration is followed dorsalward from the pyramidal tract to the dorsolateral angle of the tegmentum, ending at the level of the facial nucleus, beyond which point we cannot demonstrate it. No decussation to the extralateral nucleus was noted.

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## DISCUSSION

Dr. Adolf Meyer of Baltimore said that he considered this a very interesting question. The fact remained, however, that Dr. Bagley in his experiments did not ever get any passing over of fibers of the pyramidal tract for the contralateral functions in the cranial segments. It was probable that the pyramidal fibers reached the segment and that perhaps in the intrasegmental working the determination took place as to which responses were going to come, the ipsolateral or the contralateral, although in the cerebral cortex there appear to be different regions from which these tendencies could be provoked.

# PARALYSIS OF ASSOCIATED LATERAL MOVEMENTS OF THE EYES

## A SYMPTOM OF INTRAPONTILE LESION *

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PHILADELPHIA

Now that the cranial cavity is being opened by surgeons with less and less reluctance, the differential diagnosis between a lesion within the brain substance and one on the surface becomes of increasing importance. Especially is this true of tumors of the posterior fossa, in which field have been made some of the most recent advances in the art of intracranial surgery. Cushing's book, "Tumors of the Nervus Acusticus" indicates what measure of success has been attained.

Since cerebellopontile angle tumors are accessible, and intrapontile tumors inaccessible, naturally the diagnosis between them should anticipate operation. Tumors of the angle by pressure can cause many of the paralyses, anesthesias and ataxias caused by intrapontile lesions. There is, however, one symptom very characteristic of a lesion within the pons that has not been successfully produced by an acoustic tumor. Though Frankl-Hochwart, Alexander, Cushing and Henschen have reported cases in which associated movements of the eyes were interfered with, there has been no case of tumor in the cerebellopontile angle causing clear-cut paralysis of associated lateral movements of the eyes with preservation of the convergence reaction of the internal recti. The following case will show the importance of recognition of the symptom.

### REPORT OF A CASE

*History.*—On Dec. 16, 1917, Miss S. K., a white woman aged 59, was admitted to the service of Dr. Spiller at the Hospital of the University of Pennsylvania, complaining of dizziness and diplopia. For the last three and a half years she had not been well, being troubled at first by frontal headaches and attacks of vomiting. About two years ago a hissing sound developed in her left ear and a month later she noticed that she was deaf in that ear. She began to stagger while walking, and this became progressively worse until she had to stop work. In February, 1917, she noticed that the right side of her mouth drew up and that the left eye could not be closed completely. Vision at a distance was blurred and recently she had had diplopia. The left side of her face had become numb. She could chew well but she had difficulty in swallowing, and when attempting to drink fluids escaped from the corner of her mouth. The left side of her tongue became numb, and things did not taste the same on the two sides. In November her voice took on a quiver. There was no weakness of the limbs.

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* From the University Hospital.

She had had bronchial trouble at the age of 18 for about eighteen months and typhoid fever at the age of 38. Her social and family history were negative.

*Physical Examination.*—This revealed an emaciated woman of good mentality. The cranial vault was normal; neither drum head showed disease. Hearing was normal on the right; the left ear was deaf to air and bone conduction.

Face: The left brow muscles contracted poorly. The left eyelid could not be completely closed and showed fine fibrillary twitching.

Eyes: There was slight rough nystagmus on looking straight ahead and at times a slight outward squint for a few moments. Looking far to the right started slow horizontal nystagmus with the rapid component to the right. Looking to the left the rapid component was to the left. Looking upward caused nystagmus both vertical and rotatory, with the rapid component up. The pupils were equal and reacted normally to light and in accommodation. Vision was impaired in both eyes, more so on the left. Fundus examination showed only slight pallor of the nerve heads and slight diminution in the size of the arteries.

Fig. 1.—The convergence of the eyeballs when associated movement to the left was impossible.

Mouth: The left corner of the mouth could not be drawn up and attempts to whistle showed a flat left side. The tongue was protruded in the midline. Taste was normal for bitter, sour and sweet, but salt was miscalled on both sides. The gag reflex was diminished. The masseter did not contract as strongly on the left, and the jaw deviated to the left.

Chest: At the right apex there was harsh breathing with prolonged expiration. The heart was normal as were the abdomen and extremities.

Gait and Station: The gait was uncertain, not spastic. There was difficulty in standing with the eyes open, not increased by closing them. The hands had a coarse tremor.

Reflexes: Biceps and triceps reflexes and the knee and ankle reflexes were bilaterally overactive. There was patellar clonus on both sides and ankle clonus on the left. There was no Babinski sign or abdominal reflex.

There was a tendency to hypermetria; there was no adiadokokinesis. Stereognostic perception was good, sensation normal.

Blood, urine and cerebrospinal fluid were normal. The Wassermann reaction was negative.

Eye Report (May, 1918): There was a decided horizontal nystagmus, most marked in excursion to the right. The pupils were widely dilated (homatropin) the right more than the left. The right eye was normal. The left fundus was slightly hazy, probably due to slight changes in the corneal epithelium from

Fig. 2.—Base of brain showing glioma of pons.

exposure. There was paralysis of the left external rectus and of the left orbicularis palpebrarum. The corneal reflex was diminished on the left. Vision in the right eye was 6/12, in the left 6/15.

Nose and Throat Report: Distinct anesthesia of the left side of the soft palate, base of the tongue and larynx was present. There was no actual paralysis of the palatine and laryngeal muscles, but they did not contract well.

Ear Report: There was almost complete nerve deafness on the left side.

Vestibular Report: There was spontaneous nystagmus as described in the foregoing. Turning to the right stopped the spontaneous nystagmus for ten

seconds. Turning to the left increased the large existing nystagmus for twenty-five seconds. The douche gave no nystagmus on either side with the head straight. With the head back there was a marked reaction upward on douching the right ear with a tendency to conjugate deviation to the left. On douching the left ear, the head being thrown back, there was no reaction. Past-pointing was spontaneous to the left. This was little changed by rotation in the chair.

*Course.*—A diagnosis of tumor of the cerebellopontile angle was made and operation suggested. There was some hesitancy about operating until the condition of the patient was better. In the fall of 1919 exploration

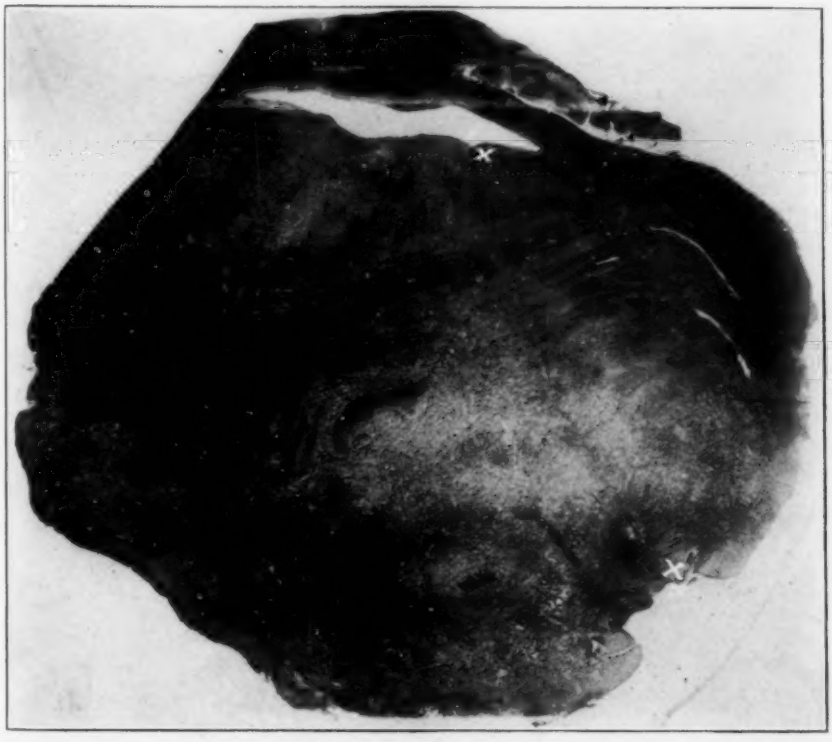

Fig. 3.—Section of pons showing glioma; *x*, raphé. The architecture of the pons has been almost completely destroyed by the tumor. In comparison note the well defined markings of the cerebellum.

was decided on, when Dr. Spiller found paralysis of associated movements to the left with preservation of the power of convergence. Operation was immediately abandoned, it being certain that the lesion was intrapontile and inoperable. The symptoms steadily progressed, the patient grew gradually weaker, and died on May 6, 1920, having been bedridden for about two months. The day before death, though her mentality was greatly reduced, she still recognized people. The grip was fair and well coordinated; her speech was almost unintelligible. The paralysis of associated lateral movements to the left was unchanged and there was still slight power of convergence (Fig. 1).

*Necropsy Examination.*—This revealed a glioma of the pons which was much enlarged by the tumor (Fig. 2). Over the anterior surface of the left half there was a flattened mushroom growth extending into the left cerebellopontile angle, apparently not infiltrating the left cerebellar hemisphere. The right half of the pons was also infiltrated.

On sectioning the hardened brain-stem through the pons above the entrance of the fifth nerve, the left side was found much larger than the right, and the median raphé distorted (Fig. 3). The fourth ventricle was reduced to a

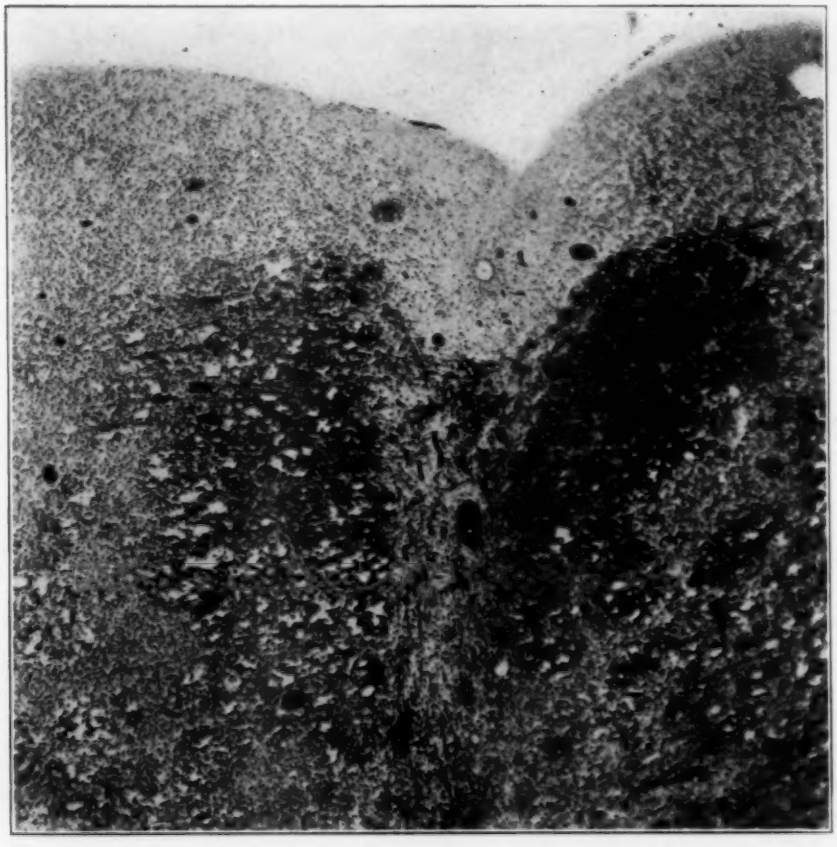

Fig. 4.—Photomicrograph of posterior longitudinal bundles showing marked degeneration on the left.

narrow slit and nearly occluded at a higher level although there was no actual obstruction since the lateral ventricles were not dilated. The growth was located principally on the left side in the ventral portion, though it involved the right pyramid and also the dorsum of the pons and part of the floor of the left half of the fourth ventricle. It extended through the brachium conjunctivum into the left lobe of the cerebellum.

The centripetal fibers in the dorsum of the pons retained their myelin sheaths to a large extent, but the entire ventral portion of the pons was replaced by

a diffuse infiltrating gliomatous growth that had destroyed the myelin sheaths. The tumor was cellular, most of the cells being spindle-shaped, with large vesicular nuclei staining deeply. Blood vessels were moderately numerous, with thin walls and large caliber. There was no distinct boundary to the growth, but a gradual transition from normal nervous substance to tumor tissue. A few myelin sheaths could be seen well within the boundaries of the tumor (Fig. 3).

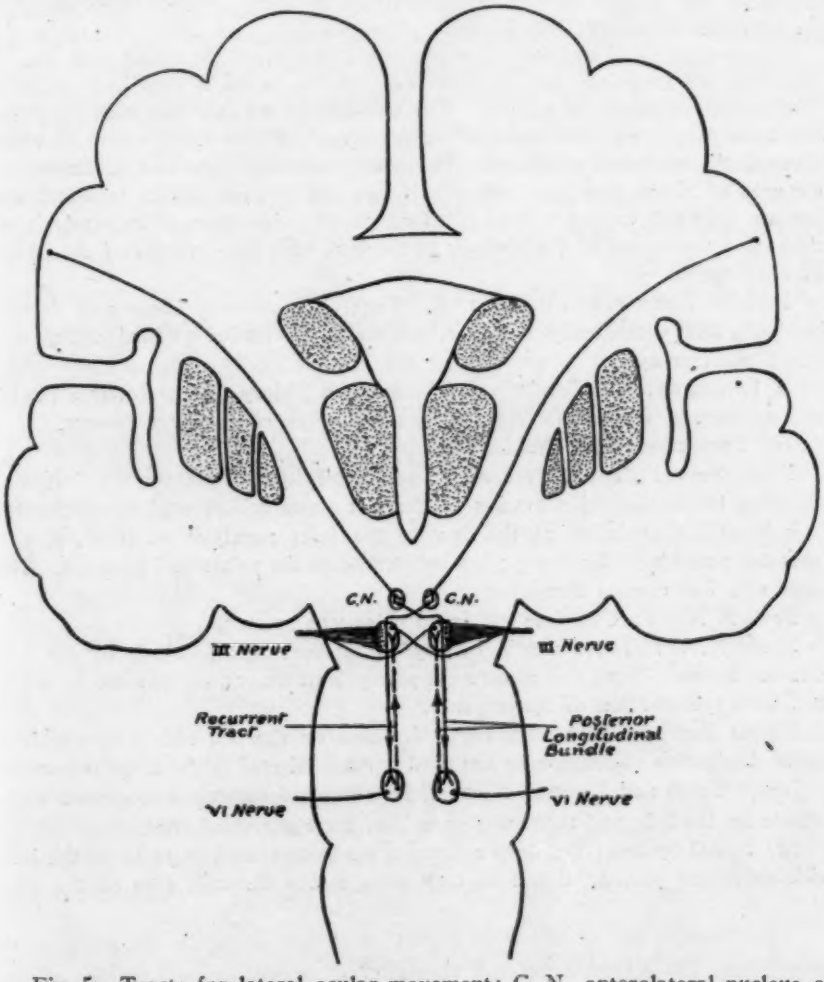


Fig. 5.—Tracts for lateral ocular movement; C. N., anterolateral nucleus of Darkschewitsch (modified from Piersol).

Of special interest was the posterior longitudinal bundle which could be seen with the naked eye to be smaller and paler on the left than on the right. In Weigert preparations, the left fasciculus, while not infiltrated by tumor cells at the level examined, was seen to be reduced in size, vacuolated, and replaced to a large extent by glia. The right fasciculus, while not entirely normal, showed much less advanced changes (Fig. 4).

The left sixth nerve was found to be smaller and paler and more translucent than the right one. The left seventh and eighth nerves showed the same degenerative changes.

Sections from the cords showed no visible degeneration of the tracts. The ventral horn cells contained no more than the physiologic amount of pigment. The pia was hyperplastic but not infiltrated.

SUMMARY

Notes on Condition, Jan. 22, 1920:

Chronology of Symptoms: For five and a half years there had been frontal headache and vomiting, and for four years hissing in the left ear and deafness. The patient staggered in walking. The left side of the face had been paralyzed for three years. She had diplopia two years ago. There was a reflux of water through the nose and dysphagia. Her voice quivered. She had dizziness and dimness of vision. A year and a half ago she became unable to stand and leaning forward caused vomiting. Two months ago there was paralysis of associated movement of the eyeballs to the left, with preservation of the power of convergence.

Positive Neurologic Findings: A. General Pressure: There was frontal headache and occasionally vomiting, sometimes projectile. Visual acuity was 6/22.3 in either eye.

B. Localizing: (1) Cerebellar: There was a history of "cerebellar attitude" and nystagmus, vertical, lateral and rotatory. Hypermetria was present.

(2) Extracerebellar: Cranial Nerves:

Fifth Nerve: There were slight subjective hypesthesia on the left and objective diminution of sensation in the left supra-orbital region; neuroparalytic keratitis; deviation of the jaw to the left; paralysis of temporal and masseter muscles with atrophy; insensitiveness of the palate and pharnyx. The right side was normal throughout.

Seventh Nerve: Complete left facial palsy was present.

Sixth Nerve: There was a history of diplopia and paralysis of the left external rectus. There was also recent paralysis of associated movements to the left, with preservation of convergence.

Eighth Nerve: There were nerve deafness on the left side with tinnitus; recent diminution of hearing on the right; greatly altered labyrinthine responses.

Ninth, Tenth and Eleventh Nerves: Dysphagia, dysarthria and ageusia were present on the left, and there was paresis of the right vocal cord.

(3) Spinal System: The deep reflexes were exaggerated, more so on the left, with ankle and patellar clonus on both sides and a Babinski sign on the left.

The feature of prime importance was the paralysis of associated movement for it rendered the thought of operation untenable. The symptom was striking. Barring nystagmus, the eyes could be moved normally to the right, upward and downward, but movements to the left of the midline were impossible. Yet the patient could converge to the physiologic limit, that is to say, the internal rectus of the right eye was paralyzed for associated movement to the left, but not for the same movement in convergence (Fig. 1). At rest both eyes were in the primary position.

The syndrome is known by various names in other languages; in French: "Paralysie des mouvements associés de lateralité des globes oculaires"; in German: "Seitliche Blicklähmung." The French sometimes term it "Syndrome de Foville."

The first mention of it in the literature was made by Foville in 1858, when he described a typical case, with paralysis of the left side of the face and right side of the body and paralysis of associated movement of the eyes to the left. Unfortunately necropsy examination was not made, but his name has been connected with the syndrome. Foville considered that there was paralysis of the right internal rectus, and it was Féréol who first pointed out that this was only a functional paralysis, and that there was preservation of the power of convergence. Necropsy examination in his case showed a tubercle in the dorsum of the pons on the left side. Féréol also noted that when the left eye was closed, the right eye could be moved freely in all directions and that it was only in associated movements that there was inability to look to the left. Many other investigators have since made contributions to the study of this syndrome.

## THE HIGHER CENTERS

The movements of the eyes to the sides demand a fine coordinating mechanism for the continued maintenance of binocular vision. This mechanism consists of two parts, the voluntary or cortical centers, and the reflex or pontile centers. The locations and functions of each are:

*Cortical.*—Grünbaum and Sherrington, following Beevor and Horsley, found an area in the middle and inferior frontal convolutions, excitation of which caused conjugate deviation of the eyeballs to the opposite side. Sherrington [19] concluded that the taxis of muscles lying to the right of the median sagittal plane was entrusted to the left hemisphere, and *vice versa.* Associated movements of the eyes have also been obtained by stimulation of the occipital cortex and a visuomotor area has been postulated. Also, in the temporal lobe there is an area, stimulation of which causes conjugate movements of the eyes to the sides, the so-called auditomotor area.

Bernheimer [15] presents evidence that the gyrus angularis is an important center for associated movements of the eyes, but his stimulation of this area may have reached the underlying fibers of the optic radiations and had an effect similar to that from stimulation of the occipital cortex. Most investigators believe that the foot of the second frontal convolution exercises control over lateral associated eye movements (Bielschowsky).

Clinically, unilateral lesions of the upper tract for conjugate movement of the eyes are relatively frequent and the behavior of the eyes after a cerebral accident may indicate the seat of the lesion. The most common symptom is conjugate deviation with inability to move the eyes to the opposite side. This may be irritative or paralytic. For instance,

it forms a part of many epileptic attacks and is almost constant in jacksonian fits affecting the muscles of the head. In these (irritative) cases the eyes are directed away from the side of the lesion. As a paralytic phenomenon conjugate deviation occurs in apoplectic seizures, especially when the second and third frontal convolutions are affected. Klaas describes such a case in full and refers to many more. In these cases the eyes are turned toward the side of the lesion and remain deviated for a varying length of time.

When the conjugate deviation occurs as part of a convulsion, it lasts only during the convulsion. In the paralytic cases also, even though the whole motor cortex or the internal capsule is destroyed, the conjugate deviation of the eyes is only temporary.

This fleeting deviation of the eyes from interference with the upper tracts contrasts with that due to destruction of the lower centers or tracts, which is permanent. When the dorsum of the pons is destroyed, for instance, there is often lasting deviation away from the side of the lesion. As the French say: "Le malade regard ses membres paralysés."

It sometimes happens that both sides of the cerebrum become softened, one after the other, in the condition known as pseudobulbar palsy. The behavior of the eyes in this condition is described by Wernicke,[35] Oppenheim [36] and others (vide infra).

Since the cerebral paralysis of associated lateral movements is merely temporary even though the center on one side is destroyed, it must be assumed that the function of lateral oculogyration is taken up by another area. That this cannot be consummated immediately is shown by the time elapsing before normal function is restored. It is supposed that the cortex of the opposite side takes on the function of the area destroyed. Lewandowsky says that destruction of one cerebral peduncle fails to cause permanent paralysis of associated lateral movements and Bielschowsky says that in some experiments in stimulating the cortex, conjugate lateral movements have been obtained to the same side, though it is admitted that these movements are usually replaced by those in the opposite direction.

When bilateral lesions affect the motor tracts for the eyes as in pseudo-bulbar palsy, there is bilateral paralysis of associated movements, but in these cases only the voluntary turning of the eyes is prevented, while the automatic and reflex movements are retained. Roth [37] and especially Bielschowsky [34] have given the following method of differentiating this supranuclear paralysis of associated lateral movements from that due to disease of the lower centers and roots: "Direct the patient to fix an object directly in front of him, and then turn his head passively to the sides. The eyes will turn to the physiological lateral limit, in a manner that was not possible through voluntary control. Sometimes in following a moving object the eyes will turn to the sides normally, yet the patient cannot voluntarily look to either side."

In these cases only the voluntary mechanism is out of order and the other centers remain intact. Thus visual and auditory stimuli are capable of causing associated ocular movements entirely beyond the control of the will. This is discussed under "Nystagmus."

*Cerebellum.*—Thomas [20] ablated half of the cerebellum of monkeys and observed conjugate deviation of the eyes to the opposite side, lasting from one to twenty days. When the vermis was intact there were no symptoms, but injury to the vermis always caused nystagmus. Gaussel [23] concludes that conjugate deviation is seen in acute lesions of the cerebellum, but not in slowly advancing ones. Paralysis of associated lateral movements without conjugate deviation is not a cerebellar symptom, but due to pressure on the subjacent centers for associated movements.

*Corpora Quadrigemina.*—Stimulation of the anterior corpora quadrigemina produces conjugate deviation of the eyes, but destruction of these bodies does not cause paralysis of associated lateral movements, and stimulation of the underlying tissues produces the conjugate movements as before. This seems to signify that the fibers for oculogyration run beneath the corpora quadrigemina and that a lesion of the corpora quadrigemina causes conjugate paralysis only when it involves the upper part of the pons (Gaussel).

From this review it may be stated that:

(1) Associated lateral movements of the eyes are possible of control bilaterally in the cerebral cortex.

(2) Unilateral lesions of the brain above the cerebral peduncles cause only temporary paralysis of associated lateral movements.

(3) The cerebellum and corpora quadrigemina are not the lower centers for lateral oculogyration.

## TYPES OF PARALYSIS

Lateral movements of the eyes require the concerted action of the external rectus of one side and the internal rectus of the opposite side; that is, of the sixth nerve on one side and the third on the other. Therefore an intimate connection between these nuclei is necessary. This connection is generally conceded to be the posterior longitudinal fasciculus. Concerning this tract Déjerine writes:

> Fibers of very early myelinization going in both directions connect the nucleus of the abducens with the oculomotor nucleus on the same side for the purpose of associating the lateral movements of the eyeballs. These internuclear fibers take their origin from small cells contained in the oculomotor and abducens nuclei and pass by the posterior longitudinal fasiculus.

The small cells in the upper part of the abducens nucleus of the right side, for instance, can bring into action the small cells of the oculomotor nucleus of the same side, and cause parallel movements to

the right. An exactly similar mechanism is elaborated for the conjugate movements to the left. Déjerine continues:

> Thus is formed a physiologic association tract, consisting of a dextrorotatory system which carries the glance to the right and a levorotatory system which carries the glance to the left, an association path which can be stimulated and activated not only by the cerebral cortex, but also by several central paths, auditory, labyrinthine, tactile, visual, etc.

It will be noticed that no mention is made of a decussation of the posterior longitudinal fasciculus between the sixth and the third nuclei. In spite of numerous attempts to establish such a fact, no satisfactory evidence of such decussation has been found. But Bernheimer [15] and others have found experimentally that the internal rectus of one side is controlled from both sides of the brain-stem, and Bruce, after a careful study of his case, in which he found ascending degeneration of the posterior longitudinal bundle ending in the oculomotor nucleus of the same side, says: "It is known that some of the fibers of the oculomotor nerve arise from the opposite nucleus. If these are the fibers to the internal rectus there need be no decussation of the posterior longitudinal bundle."

It was suggested that the fibers of the internal rectus might arise from the nucleus of the opposite external rectus, but in every case of paralysis of associated lateral movements of the eyes in which there has been no direct involvement of the oculomotor nucleus, the oculomotor nerve has been normal. Therefore the connection between the abducens nucleus and the internal rectus muscle must be indirect.

In paralysis of associated lateral movement ordinarily the internal rectus of the opposite side is paralyzed for this function only. The eye that cannot be brought beyond the midline in looking to the side, will roll in until the cornea reaches the inner canthus, in a strong effort at convergence. But in some cases convergence also fails, and Spitzer concluded that there were some fibers for convergence reaching as far down as the abducens nucleus. This loss of the power of convergence is noted in many cases in which large lesions have greatly distorted the whole pons. In our case, on Nov. 11, 1919, when paralysis of associated lateral movements was first noted, convergence was preserved. By March, 1920, it had failed until the right eye scarcely passed the median line, and at last it practically disappeared.

Lewandowsky says that convergence is a very unstable mechanism, and its loss from lesions below the oculomotor nucelus is a pressure effect rather than one of direct involvement.

The before-mentioned condition first noted by Féréol, that covering the eye that is paralyzed for external rotation allows the other to perform normal movements of adduction, has aroused a good deal of discussion. Some have postulated a separate tract from the cortex

to the internal rectus that would account for the power of the single muscle when binocular vision was excluded, but, as Bielschowsky [2] points out, it is a fundamental conception that the lateral movements of the eyes are always associated.

> There is no point in the cortex—at least in man—from which isolated movements of one eye can be obtained. Also clinicopathologic observations teach that in unilateral lesions of the cortex, especially the hemispheres, there are always bilateral disturbances of eye movements. Both eyes seem to be, in motor as well as in sensory respects, a single organ.

To explain the activity of the eye in monocular vision that is paralyzed for binocular vision, some other hypothesis is needed. The phenomenon is best explained by the maintenance of the power of convergence, as was insisted by Bielschowsky. He pointed out that no mention was made of the behavior of the eye under cover, whether it rotated inward in conjunction with its fellow, or whether there were pupillary changes corresponding to the reaction of accommodation. He mentions several ways in which seemingly dissociated movements of the eyes may be obtained, but they all hinge on the convergence mechanism. Later Neumann [104] found that there was inward rotation of the covered eye, and narrowing of the pupil, thus confirming Bielschowsky's opinion.

An example of the opposite of this phenomenon has been described by Bernheimer.[49] In his case, covering the eye whose internal rectus was paretic for associated lateral movements, allowed the external rectus of the opposite eye to functionate normally. Bernheimer seems to have concluded (Bielschowsky [2]) that when one eye is covered the impulse to lateral movement is carried to the eye muscle nuclei by other routes than during binocular tests. In this condition there is no other explanation beyond that of a disputed divergence mechanism, so that the maintenance of power in the external rectus for monocular vision with the paralysis for binocular vision is stronger evidence for the individual innervation of the eye muscle nuclei. But the basic principle of parallel conjugate movements controlled by a supranuclear center still holds, and Bielschowsky, in discussing the case, says:

> I would rather believe that in cases like Bernheimer's, the paralysis of the associated muscles was not absolutely equal, and that the least damaged muscle would react for monocular tests when it would not for binocular tests, because abhorrence of the inevitable diplopia resulting from unequal contraction of the associated muscles would be sufficient cause for a complete failure of impulses to associated lateral movement.

Including this case of Bernheimer's, there are, then, four different manifestations of paralysis of the external rectus in relation to the internal rectus of the opposite side: 1. The cerebral or supranuclear in which in cases of pseudobulbar palsy the eyes cannot be made to move to the sides through control of the will, but yet are able to be brought

into extreme deviation by tests for reflex movements of the eyes. 2. Paralysis from involvement of the nerve root or the nerve itself in its course through the cranial cavity. In this condition the internal rectus of the other eye is not affected. 3. Paralysis of associated lateral movements with maintenance of the power of convergence, the nuclear type of paralysis that forms the subject of this paper. 4. The type reported by Bernheimer, in which there is paralysis of associated lateral movement, yet with the covering of the sympathetic eye, the external rectus of the other eye is functionally active. The inference that may be drawn from this important case will be considered later.

### THE LOWER CENTER

There is a mass of conflicting evidence and theory concerning the existence of a center in the pons governing conjugate lateral movements of the eyes. The chief objection to its presence is the failure to find any definite group of cells that can be called a center (Marburg) although von Monakow, and later Bernheimer [1] describe scattered columns of cells in the neighborhood of the aqueduct of Sylvius that are supposed to be in connection with the posterior longitudinal bundle, and through it with the eye muscle nuclei. Parinaud,[13] Poulard, Raymond [116] and Guillain accept this. Arguing from analogy, it may be said that there is no demonstrable center apart from the nuclei of the respective nerves for the movement of convergence or for the symmetrical action of the muscles of the larynx, yet there must be a very close connection between the two sides of the brain for the performance of these acts. Most authors consider the center for associated lateral movements, if there be such a group of cells, to be in the neighborhood of the abducens nucleus. Uhthoff [10] is the chief exponent of this conception from examination of the cases of Féréol, Wernicke [140] and others.

Grasset and Gaussel, Hunnius,[91] Wernicke,[140] Benvenuti, Bach and others believe that the center is the sixth nucleus itself. But Spitzer points out that the cases of Quioc, Garel, Hunnius [93] and Senator showed no lesions of the nucleus itself; and Uhthoff mentions the case of Siemerling, one of taboparesis of many years' duration, as one in which the sixth nucleus was almost completely destroyed without paralysis of associated lateral movements of the eyes. Siemerling summarized the case incorrectly, however, for in the full report of the case, not only is there no mention of paralysis of the external rectus, but both abducens nuclei are reported as being untouched. Frey reported a case of bilateral abducens paralysis with preservation of vertical movements and of normal movements of the internal rectus. Necropsy showed a tubercle involving the left abducens nucleus, posterior longitudinal bundle and the intrapontile fibers of both sixth

nerves. This is the only clear case of isolated paralysis of the external rectus from a nuclear lesion that I have been able to find, and I have looked specifically for this condition, as I consider it of great importance in the question of a center. Siemerling's case is beyond consideration, and in Frey's case, in which there was paralysis of divergence and marked internal strabismus of both eyes, it would be impossible to determine paralysis of associated movements to the sides.

On the other hand, minute lesions involving the abducens nucleus and very little of the surrounding territory, but still causing paralysis of associated movements of the eyes, have been reported by Bennett and Savill, Benvenuti, Bloch and Guinon, D'Espine and Démolé, Garel, Hallopeau, Ormerod, Rohmer, Rohmer and Hoche, Seggel, and Wierzma.

Bielschowsky believes the actual center is in the tegmentum of the pons near the abducens nucleus. Lewandowsky,[6] following von Monakow,[8] considers it to be "near the abducens nucleus, anterior and close to the abducens, beside it, within it, and between it and the posterior longitudinal fasciculus," a sufficiently wide range of possibilities. Marburg, in his review of the literature, rejects the idea of an actual center, saying: "The lesion in Hunnius' case was above the sixth nucleus, that of Hallopeau's was within it, and that of Senator's was ventrolateral to the nucleus, still within the tegmentum of the pons, but neither in the posterior longitudinal fasciculus, nor in the sixth nucleus." It will be seen, however, in the case reports at the end of this paper, that in Senator's case there was oculomotor paralysis of the other eye, so that it cannot be considered one on which to base a conclusion as to the existence of a center.* Marburg concludes that:

> No one of the different centers proposed by different authors can explain all the manifestations, so that it seems best entirely to eliminate the idea of a center for lateral associated movements (Blickzentrum). Paralysis of associated lateral movements speaks for a lesion in the tegmentum of the pons, lying mostly medial and dorsal, usually involving the posterior longitudinal bundle and the abducens nucleus.

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*This type of paralysis may be termed spurious paralysis of associated movements. It is true that neither eye can be moved beyond the midline to that particular side, but it is due to actual paralysis of the internal rectus on one side and of the external rectus on the other. It may be differentiated from the true form by recognition of the ptosis, the limitation of the other movements, and especially by the failure of the convergence reaction. It is peripheral rather than central. Since this paper was written I have studied a case of basilar meningitis in which this condition was present. Neither eye would move to the right beyond the midline, but there was oculomotor palsy on the left side, with ptosis, and limitation of all except outward movement in that eye, whereas in the right eye there was a sixth nerve paralysis. There was no convergence reaction obtainable in the left eye.

Practically all authors agree that the posterior longitudinal bundle carries the impulses for lateral movements of the eyes between the third and the sixth nuclei, although Lewandowsky describes another connection that he has found in lower animals between the two nuclei, and Bruce speaks of an ascending strand of degenerated fibers that split off from the posterior longitudinal bundle and was lost to view. The posterior longitudinal bundle is so well defined in contradistinction to the vagueness of a special center, that Marburg has suggested that it is the fibers themselves, and not any nucleus, destruction of which causes the symptom of paralysis of associated lateral movements. But the fibers of the bundle must come from cells, and these cells, whether they are grouped or scattered, constitute the center for associated movements. Moreover, it has been shown by Seggel that many of the fibers making up the bundle arise from cells in the upper part of the abducens nucleus.

I think the evidence furnished by the cases reported is insufficient to exclude the abducens nucleus as the center for the associated movements to the same side. The posterior longitudinal fasciculus certainly is the tract by which impulses are carried both to the nucleus and away from it, a combined afferent and efferent tract. It is almost certain that it is by this route that fibers from the cortex reach the abducens nucleus, and Spitzer, Bertelsen and Rönne, Bruce and others insist, though Lewandowsky opposes this view, that it carries ascending fibers from the abducens nucleus to the oculomotor nucleus. Since the ascending and descending fibers lie side by side in the posterior longitudinal bundle, usually both sets are caught by any lesion involving the posterior longitudinal bundle, but Bernheimer's case, and others that will be mentioned later, seem to show that the recurrent tract can be involved without the descending one.

With the foregoing in mind, the anatomy of the tracts for conjugate eye movements may be mapped out, and the four types of paralysis of the external rectus with relation to the internal rectus of the opposite side set on an anatomic and physiologic basis.

### TRACTS FOR LATERAL EYE MOVEMENTS

1. The motor tract for associated movements of the eyes, for instance to the right side, begins in the cerebral cortex, mostly of the left side, and runs down through the knee of the internal capsule and the cerebral (Déjerine) peduncles as far as the posterior commissure. Here a subtotal decussation takes place, the fibers continuing down in the posterior longitudinal fasciculus, mostly of the right side. It is possible that there is a synapse for some of the fibers in the nucleus of the posterior longitudinal bundle slightly above the level of the

oculomotor nucleus. A lesion of this tract and of its fellow of the opposite side as far down as the level of the third nucleus, will cause the supranuclear paralysis, in which the eyes cannot be moved voluntarily to the sides, but will react to the stimulation through reflex paths (Neumann, possibly Bárány, Wernicke).

2. In the posterior longitudinal bundle, descending fibers run down to the level of the right sixth nucleus. As this nucleus lies almost adjacent to the bundle, there is no distinct tract connecting the two structures. A lesion of this tract or of the abducens nucleus itself will cause paralysis of associated movements to the right, and if the third nucleus is not involved there will be preservation of convergence and of vertical movements. This is the nuclear type of paralysis in which the great majority of the cases fall. Bertelsen and Rönne describe such a case in which there was a selective degeneration of only one portion of the posterior longitudinal fasciculus, that lying in the central portion of each bundle.

3. The right abducens nucleus is the origin of the peripheral fibers going to the external rectus of the right eye. Destruction of this root or of the nerve after its departure from the brain-stem will cause paralysis of the external rectus without any involvement of the internal rectus of the left eye.

4. The right abducens nucleus is also the origin of fibers running up to the oculomotor nucleus of the same side, a peripheral tract as far as the abducens nucleus is concerned, yet a supranuclear tract on the part of the third nucleus. It may be called the internuclear tract (Fig. 5). A lesion here will cause isolated paralysis of the left internal rectus for lateral associated movements, with preservation of its power in movements of convergence. Bernheimer's case comes in this category. I have found two others in which this was certain, and four more in which it was suggested. In Bielschowsky's case [2] there was paralysis of both internal recti for associated movements to the sides, with preservation of the power of the external recti and nearly normal power of convergence. In Bruce's case there was complete paralysis of conjugate movements to the left and great weakness of the left internal rectus for conjugate movements to the right. The right external rectus functioned normally. Bielschowsky's patient, who had trauma of the back of the head, recovered, but since the minute hemorrhage, which, in his opinion was located in the central gray matter, could cause paralysis of both internal recti for associated lateral movements, and no other symptoms, it would seem that the recurrent tract from the abducens nucleus to the oculomotor nucleus of the same side lay next to the raphé in each posterior longitudinal fasciculus.

It was this tract which was interefered with in Bernheimer's case. The lesion abolished associated movements of the eyes to one side, yet when the eye whose internal rectus was paralyzed was covered, the eye that failed to move outward in associated movements took on its normal function. For binocular movement, as Bielschowsky said, there was sufficient inhibition working through cortical tracts, owing to the abhorrence of diplopia, to keep both eyes from rotating, yet when the diplopia was excluded by covering one eye, the other would react to stimuli sent from the cortex.

To conclude, we may consider the abducens nucleus the center for associated lateral movements of the eyes to the same side; the posterior longitudinal bundle the tract by which efferent stimuli are carried to the nucleus from the cerebral cortex and effernt stimuli from the abducens nucleus to the oculomotor nucleus of the same side; and this oculomotor nucleus the origin of the fibers to the opposite internal rectus muscle.

### CONJUGATE DEVIATION

As was noted, conjugate deviation of the eyes is common in many lesions of the oculomotor tracts, either as an irritative or as a paralytic phenomenon. In lesions above the cerebral peduncles it is transient, as is paralysis of associated movements to the opposite side. If the lesion is irritative, the eyes turn to the opposite side; if paralytic, they deviate toward the same side.

Conjugate deviation in cerebral lesions is of little localizing value. According to Jacobi: "Transitory deviations of the eyes frequently seen after hemorrhage into any part of the brain, are due to the remote shock propagated to this nucleus" (the center for ocular rotation). Conjugate deviation is also seen in acute lesions of the cerebellum, both clinically and experimentally, due to the same "remote shock."

As a symptom of pontile lesion, conjugate deviation is apt to be permanent. Prévost, who first described the condition, found it in connection with hemorrhage into the pons.

There is a variance of opinion in assigning this phenomenon to any group of cells. Oppenheim [9] incriminates the vestibular fibers and thinks that destruction of Deiters' nucleus is accompanied by permanent conjugate deviation. Bennett and Savill believe that the sixth nucleus controls rotation of the head and eyes. In their case the lesion was only 2 mm. in diameter and situated exactly in the sixth nucleus. But fibers having their origin in Deiters' nucleus run through the sixth nucleus on their way to the posterior longitudinal bundle, fibers which are concerned, as will be seen later, with the production of nystagmus. It may have been destruction of these fibers in Bennett and Savill's

case that caused the deviation. Against Oppenheim's theory is the fact of large growths having invaded Deiters' nucleus without the production of conjugate deviation.

It seems likely that in the pons, as in the cerebrum, acuteness of the lesion determines the conjugate deviation; in slowly advancing lesions compensation is effected, whereas in acute lesions it is not and conjugate deviation results. That frequently the head participates in the deviation supports this conception. The slow-growing widely extended glioma here reported was not accompanied by deviation; in Oppenheim's case a tubercle caused deviation of the eyes alone; whereas in Bennett and Savill's case, the minute lesion, thrombosis, caused deviation of both head and eyes.

Spitzer studied a case of large tubercle in the dorsum of the pons extending slightly across the midline to involve the opposite posterior longitudinal bundle. There was deviation of the head to the left and of the eyes to the right, with paralysis of associated movement of the eyes to the left. Spitzer explained the condition by assuming that tracts for lateral movements of the head and eyes run close together, that one bundle was destroyed, causing the eye symptoms, and that the other was "disturbed caudal to the sixth nucleus where it contained more of the head-turning fibers." His microscopic drawings of the posterior longitudinal bundles show the division of the tract into three portions and the degeneration of one portion. Déjerine described a similar case but without the minute findings.

It is probable that Oppenheim is correct in assigning to Deiters' nucleus the function of reflex conjugate deviation, as will be seen in the next section, and that the degree of deviation depends on the acuteness of the lesion.

### NYSTAGMUS

When Bárány brought out his papers on the artificial production of nystagmus it was hoped that a short cut to the topical diagnosis of diseases of the brain-stem had been found. But the evaluation of these methods is yet to be made.

Douching the normal ear with cool water produces nystagmus in the opposite direction, explained by Bárány thus: Stimulation of the labyrinth excites the cells of Deiters' nucleus which send their impulses to the sixth nucleus. This reflex stimulation of the sixth nucleus causes conjugate deviation of the eyes to the side stimulated. In the extrinsic muscles of the eyeball there are large numbers of end-bulbs for the purpose of forwarding impulses of muscle sense to the central nervous system. The bulbs of the opposing muscles are stimulated by stretching and send impulses back to the brain-stem and up to the

cortical or subcortical centers. These excite impulses to contraction in order to bring the eyes back to their primary position. The movement produced by the higher center is rapid in contradistinction to the slow reflex phase caused by excitation of the labyrinth. The alternation of these two stimuli causes the jerky oscillatory movement known as nystagmus.

The Bárány method is of use in diagnosing:

1. Destruction of the labyrinth, the vestibular nerve, or Deiters' nucleus. There is no movement of the eyes.

2. Peripheral paralysis of the external rectus. Only the unaffected eye moves.

3. Supranuclear paralysis of associated lateral movements of the eyes. In these cases there is slow conjugate deviation to the side of the stimulation. The path to and from the subcortical center is cut off, and the rapid phase of the nystagmus is absent.

How far it will be of value in detecting a lesion of the so-called nuclear tract, the posterior longitudinal bundle, is as yet undetermined.

Bárány himself studied a case of syphilitic infiltration of the corpora quadrigemina extending into the pons in which there was paralysis of associated movements of the eyes to both sides with partial oculomotor paralysis. The reflex lateral movements were preserved, and vestibular stimulation caused conjugate deviation instead of nystagmus. Brunner [60] found no vestibular reaction in his case in which there was paralysis of associated movements to the right, and necropsy showed a tubercle involving the triangular vestibular nucleus as well as the fillet and the posterior longitudinal bundle. Neumann [35] reported a case in which the lesion was similar to but not so extensive as Bárány's, in which there was absence of voluntary, but preservation of reflex, associated ocular movements, and in which stimulation of the labyrinth produced conjugate deviation instead of nystagmus. There was no necropsy examination. In the case which I present there was no nystagmus on douching the left ear, while on douching the right with the head thrown back there was a marked reaction upward and a tendency to conjugate deviation to the left. (This was before there was any paralysis of associated lateral movements.) Thus, there was probably destruction of Deiters' nucleus or its fibers, or of the vestibular nerve on the left side, no reaction being obtainable; and interference with the fibers on the right side coming from the cortex to provide the rapid phase of the nystagmus. The extent of the destruction could not be determined accurately in the sections on account of the characteristic mode of infiltration that is a feature of gliomatous tissue.

DIFFERENTIAL DIAGNOSIS

With an understanding of the tracts for the various movements of the eyes and the abnormalities of position and movement that take place as the result of interference with these paths, the differential diagnosis between lesions within and those outside of the pons becomes possible. Sufficient has been said concerning the paralyses of associated lateral movements of the eyes from lesions of the cerebrum, cerebellum and corpora quadrigemina to give indications for the diagnosis between lesions of the supranuclear tracts and the pontile tracts. It may be well to state, however, that lesions in the neighborhood of the anterior corpora quadrigemina cause paralysis of movements of elevation and possibly depression, as well as of associated lateral movements.

The differential diagnosis between a lesion of the pons itself, and a tumor lying in the cerebellopontile angle is now to be made as being of greatest importance in deciding for or against operation. Paralysis of ocular muscles, especially of the external rectus, is a common symptom in tumors of the acoustic nerve and in endotheliomas of the cerebellopontile angle. Interference with other movements of the eyes and with combined movements is of relatively frequent occurrence. Henschen found disturbances of motor nerves to the eye in ninety out of 125 cases of angle tumor. In fifty cases there was nystagmus in looking toward the side of the lesion. Ten cases showed paralysis of associated lateral movements of the eyeballs, or "something like it," and Henschen modifies this statement by saying that the paralyses were not sharply defined, and that this is not to be considered a part of the symptomatology of angle tumors. On the other hand, Lewandowsky says that "Tumors particularly can cause the symptom of paralysis of associated lateral movements of the eyes by influence at a distance (Fernwirkung), for instance through pressure on the pons from the side, or from the fourth ventricle." Urbantschitsch reports a case of otitis media in a girl of 8, who later developed an abscess in the cerebellum the size of a hen's egg. Here there was paralysis of associated movements of the eyes and of convergence. Cushing gives detailed descriptions of the behavior of the eyes. In one case there was "definite skew deviation"; in another, "conjugate deviation poorly sustained," and in a third, "conjugate deviation possible only to the right, and then with nystagmus; almost complete ophtalmoplegia."

That pressure at a distance from large tumors can interfere with conjugate movements of the eyeballs is certain, but clear-cut paralysis of associated lateral movements with preservation of the power of convergence, means a lesion of the posterior longitudinal bundle. This tract lies just to the side of the raphé of the pons, immediately under the floor of the fourth ventricle and the gray matter of the aqueduct

of Sylvius. Hence it is in one of the most inaccessible portions of the brain, quite beyond the reach of surgery.*

In closing it may be well to quote some remarks of Spiller [109] on a case he studied in 1903. It was this case he recalled when examining our patient. He says:

> I think it well to emphasize the importance of paralysis of lateral associated movement of the eyeballs in clinical diagnosis. In such a case as the one described in this paper there might be some doubt whether the symptoms were caused by a tumor on the pons or by a tumor within the pons. As we have for some time past been trying to remove by operation a tumor upon the pons, or in the cerebellopontile angle, it is evident that if we could find a clinical sign indicating that the tumor was intrapontile, we would consider operation inadvisable when this sign was present. Such a sign I believe we have in paralysis of lateral conjugate movements of the eyeballs, and I should be unwilling to recommend operation for the removal of a pontile tumor if this form of ocular paralysis were present.

### REPORT OF CASES

GROUP 1.—*Conjugate deviation, simple and transitory, from lesions of the upper tract.* Three cases (Dufour, Grasset,[84] Klaas).

Dufour: A woman, aged 37, had had a stroke with hemiplegia three weeks before and came into the hospital comatose and aphasic. Head and eyes deviated to the left. There was right homonymous hemianopsia. "She fixes, and follows with her eyes an object which is shown to her on the left side. Most often she stops looking at it when it goes to the right." She could make her eyes go to the extreme right by this method.

Necropsy showed a large area of softening in the left lenticular nucleus, the left internal capsule, the caudate nucleus and the surrounding white matter. Farther back the softening destroyed the retrolenticular segment of the capsule and the optic radiations.

GROUP 2.—*Paralysis of associated lateral movements of the eyes for volitional movements but retention of them in reflex movements; cases of pseudobulbar palsy.* Five cases (Wernicke,[85] Anton, Oppenheim,[86] Roth, Neumann.[35])

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* The epidemic of so-called lethargic encephalitis has brought into prominence the question of the behavior of the eyes. In this disease there is little meningeal involvement and it is probable that after escaping from the brain-stem the nerves are relatively free from danger, but in their course within the brain-stem, as Boyd has shown, the nerves may be compressed and their function abolished by the greatly swollen vessels, the perivascular round cell infiltration, and the edema. (Boyd reported this at the First Annual Meeting of the Association for Research in Nervous and Mental Diseases.) Should the same process occur in the floor of the fourth ventricle in the neighborhood of the posterior longitudinal fasciculus, we might expect transitory or permanent paralysis of associated lateral movements. This has rarely been observed. Barker reports in a personal communication the occasional mention in the literature of inability to move the eyes laterally, and I have observed a case in which there was paralysis of downward associated movements. On the whole, however, the syndrome of the posterior longitudinal fasciculus may be said to be of rare occurrence in the course of epidemic encephalitis.

Neumann: A man, aged 41, had difficulty in maintaining balance, and dimness of vision on looking to the sides. He had ataxia of the left arm, increased patellar reflexes, falling in any direction, usually forward. There was paralysis of associated lateral movements to the left, with marked weakness in movements to the right, but only for voluntary movement. "If the patient fixes an object which is moving, the eyes can be brought into the lateral angles." When the head is turned passively, the same movement results. There was no nystagmus on stimulation of the labyrinth, but the Bárány tests resulted in conjugate deviation.

GROUP 3.—*Unilateral paralysis of associated movements of the eyeballs from a pontile lesion, without deviation.* Twenty-nine cases (Annuske, Ballet,[42] Benvenuti, Bernhardt, Bleuler, Bruns, two, Cestan, Crohn, Féréol, Foville, Grasset,[85] Henneberg, Hery, Huguenin-Hofstetter, Hunnius,[91] Jolly, MacGregor, Meyer, Neumann,[104] Leyden, Parinaud, two, Potts and Spiller, Poulin, Raymond,[135] Raymond and Cestan,[137] Thompson, Johnson and Ferrier, Wierzma).

Féréol: There were hemiplegia of the right side, vomiting and headache, all of long standing. Intelligence and speech were not impaired. The right eye could be moved by itself freely, but in associated movements it would not move to the left beyond the midline. Convergence was maintained.

Necropsy examination revealed a tubercle the size of a cherry in the tegmentum of the pons making a bulge into the fourth ventricle. Beneath the surface, the lesion extended slightly beyond the midline.

Neumann: A boy, aged 4, in August, 1917, developed paralysis of the left abducens. By December he had left facial palsy, especially of the lower half. Right hemiplegia came on, and later paralysis of associated movements of the eyes to the left. There were bilateral vestibular disturbances. The muscles of mastication of the left side were paralyzed.

Necropsy revealed that all but a small part of the left half of the pons was a soft caseous mass. There were tubercles also in the cerebral peduncles and in the cerebellum.

Potts and Spiller: A man, aged 55, had marked weakness of the right arm and leg and weakness of the muscles of the left side of the face except of the orbicularis palpebrarum; also of the muscles of mastication. There was paralysis of associated movements to the left. Sensation of pain, touch, heat and cold was lost on the right side of the body. There was anesthesia of the left side of the face. Astereognosis and ataxia were present, more marked in the right hand.

Necropsy revealed above the entrance of the fifth nerve a tubercle in the tegmentum of the pons extending into the pyramidal tract on the left side. The left posterior longitudinal bundle was directly involved in its upper part. The fifth, sixth and seventh nerves of the left side showed degeneration.

Wierzma: A girl, aged 10, had left facial palsy, paralysis of associated movements to the left and of the left abducens. Convergence was preserved; the extremities were not affected. She complained only of headache.

A tubercle the size of a pea involving the sixth and seventh nuclei of the left side was found at necropsy.

GROUP 4.—*Paralysis of associated movements of the eyes to one side with conjugate deviation to the opposite side.* Forty-three cases (Ballet,[41] Beevor,[46] Bennett and Savill, Bloch and Guinon, Bristowe, Broadbent, Déjerine, five, Desnos, D'Espine, D'Espine and Démolé, deVincentiis, Dimmer, Finlayson, Finny,

Garel, Graux, Hallopeau, Leyden, M'Aldowie, Mierzejewsky and Rosenbach, Mills, Oppenheim,[180] Parinaud, Peltier, Quioc, von Rad, Raymond,[115] two, Redlich, Rohmer, Rohmer and Hoche, Smith, Spitzer, Steinert, Thomas, Touche, two, Wernicke, Winkler).

Bennett and Savill: A woman, aged 67, had had a stroke with complete paralysis of the left arm. Two months later she woke up with her head and eyes deviated to the right. There was slight left facial paresis. There was paralysis of associated movements to the left, with preservation of the power of convergence and pupillary reactions. The head could not be turned to the left. Hearing in the left ear was poor. She died a month later.

Softening in the right ascending frontal convolution and an area of softening one-tenth inch (2.54 mm.) in diameter, limited to the sixth nucleus, were found at necropsy.

D'Espine and Démolé: A boy, aged 7, suffered with headache, loss of appetite and general malaise. He developed deviation of the head and eyes to the left, with paralysis of associated movements to the right. Complete right facial palsy was present. "By violent effort" the left eye could be moved in slightly, with resulting diplopia. Symptoms of tuberculous meningitis developed and he grew weak in the left arm. Death resulted in six months.

Generalized tuberculosis, tuberculous meningitis, multiple tubercles of the cerebrum, cerebellum and brain-stem were revealed at necropsy. A node 4 mm. in diameter occupied the eminentia teres. "On the right there is nothing left of the abducens nucleus but three or four cells" (in one cross-section). The right facial nerve was degenerated. The external border of the posterior longitudinal fasciculus was degenerated.

Hallopeau: A woman, aged 36, with endocarditis, pregnant eight months, had violent headaches one day. The next day there was deviation of the head and eyes to the right, and paresis of the left side of the face, both upper and lower portions. Her eyes would not go to the left in associated movements. She suffered from vertigo. She had hyperesthesia of the left side of the face and weakness of the right arm and leg. Internal squint developed in the left eye. She died of asphyxia.

Vegetative mitral valvulitis and ecchymosis, 2 mm. in diameter, in the floor of the left side of the fourth ventricle, occupying the left eminentia teres, in the position of the sixth and seventh nuclei were revealed at necropsy. There was a clot in the basilar artery from occlusion of the left vertebral artery by an embolus.

Quioc: A man, aged 54, whose first symptoms were headache and vertigo, had conjugate deviation of the head and eyes to the right, with paralysis of associated movements to the left. There was no diplopia, or paralysis of the extremities. He staggered in walking.

Necropsy revealed a tumor in the left protuberance anterior to the eminentia teres, not involving the sixth nucleus, but being able by its position to interrupt the root fibers of the sixth nerve, and encroach on the posterior longitudinal bundle. By a small prolongation to the right side, the lesion cut the raphé.

Rohmer: A man, aged 38, tuberculous, whose face was turned to the left and the eyes to the right, had no sensory or motor disturbances. The eyes could not be moved in association to the left. With the left eye closed, the right could be moved in all directions.

Necropsy revealed tubercles on the surface of the cerebrum and in the interpeduncular space. One tubercle was limited to the gray nucleus of the abducens on the left side.

Spitzer: A man aged 34, in the spring of 1896 had difficulty in looking to the left, and had vertigo on turning the head in that direction. The eyes were deviated to the right, and he had diplopia. He was troubled with headache and his health failed. In September the head deviated to the left and the eyes showed slight deviation to the right and could not be moved to the left in association. There was weakness of the left side of the face above and below. Convergence was limited. There was excessive salivation and moderate spasm of the muscles of mastication.

Necropsy revealed tuberculosis. There was a solitary tubercle in the floor of the fourth ventricle, centered about the triangular acoustic nucleus in the left side, extending over the midline in the deeper area. Medially the tumor involved the posterior longitudinal bundle on the left and to a slight extent on the right. It also involved Deiters' nucleus, the left abducens nucleus, the left facial nucleus, and the upper part of the dorsal vagus nucleus.

GROUP 5.—*Bilateral paralysis of associated movements of the eyes from lesions involving both posterior longitudinal bundles.* Twenty-three cases (Avramesco, Beck, Bertelsen and Rönne, Bischoff, Bleuler, Bramwell, Dutil, Fry, Grasset and Gaussel, Hirschberg, Jackson, Kolisch, Mabboux, Ormerod, Ransohoff, Raymond,[116] two, Raymond and Cestan,[117] two, Righetti, Seggel, Wernicke,[140] two).

Bertelsen and Rönne: A man, aged 50, had tuberculosis and syphilis, was alcoholic and had just had an attack of pneumonia. He complained of difficulty in seeing, and later in talking. He was delirious, and alcoholic neuritis set in. There was no ptosis or lagophthalmos of the eyes, the pupils gave no reaction to light but reacted well in convergence, the right being larger than the left. There was bilateral paralysis of associated movements of the eyeballs, both voluntary and reflex. The eyes were in the midline. Opening and closing the eyes caused rotatory nystagmus. Convergence was good.

Necropsy revealed poliencephalitis. At the aqueduct of Sylvius there were two small hemorrhages into the central gray matter, extending as far laterally as the posterior longitudinal fasciculi. Ganglion cells in the nucleus of the posterior longitudinal nucleus were slightly abnormal. At the level of the sixth nucleus there was an infiltration into the posterior longitudinal fasciculus on both sides. The degeneration ended with the sixth nucleus. Here there were some abnormal cells, about 25 per cent. The degeneration of the posterior longitudinal bundle was most marked in the medial portion. Except for the posterior longitudinal bundle, no degeneration was observed. The oculomotor nerve was normal.

Raymond and Cestan: A woman, aged 28, was weak on the left side and had diplopia on looking to either side. There were numbness of the mouth, anesthesia of the left hand and vertigo; hemiplegia of the left extremities and the lower part of the face, with exaggerated reflexes, astereognosis and ataxia. She had hypesthesia of the left arm, face and leg for all forms of sensation. She walked with a drunken gait and fell on attempting to turn around. There was loss of emotional control. Speech was scanning. Her eyes were in midposition and could not be moved to the sides in association, yet convergence was maintained. Optic neuritis developed late. The right side of the face became weak in both upper and lower halves.

Necropsy revealed tubercle of the pons and medulla. The third nucleus was untouched and the third nerve showed no degeneration. There was destruction of both posterior longitudinal fasciculi. The lesion spared the sixth nuclei but caught the fibers of both nerves.

Seggel: A man, aged 62, complained of failing vision on the right side, which was found to be due to choked disk. There was paralysis of the right abducens and of associated movements to the right. When the right eye was covered the left eye could be moved to the right. Convergence was good; there was no diplopia. The patient had headache and night sweats. Hearing was good. He had vertigo on turning. Later complete paralysis of the face and bilateral paralysis of the lateral associated movements developed.

Necropsy revealed a tubercle in the right side of the pons reaching over as far as the left facial fibers. Apparently it started in the right sixth nucleus and early involved the right facial fibers. Later it extended across the midline and destroyed the left sixth nucleus.

Group 6.—*Isolated paralysis of the internal rectus for lateral associated movements, from a lesion of the recurrent internuclear tract between the abducens nucleus and the oculomotor nucleus of the same side.* Three pure cases (Bernheimer,[69] Bielschowsky,[3, 81] two, Fischer); combined with paralysis of associated movements of both eyes to the opposite side, four (Bruce, Ewald, Hunnius,[91] Steinert; also Gubler and Huguenin. I could not verify these).

Bielschowsky: A man, aged 45, was hit on the head. He experienced no disturbance at first but that night there were severe headache, discomfort, dizziness and diplopia. Examination eight days later showed the right eye held shut. When it was opened it was found to be divergent 20 degrees. In looking to the sides neither eye could be adducted beyond the midline, yet convergence was nearly normal. The vertical movements were good, but attended with slight nystagmus. The external recti were functionally active in movements to the sides. The pupils were active to light and distance, and vision was good. There were no other neurologic disturbances. In a few days the divergence disappeared. The left internal rectus improved for associated lateral movements and the right rectus internus functioned normally after a year. Only slight nystagmus remained on turning the eyes to the right. There was then complete freedom of associated lateral movements.

Bruce: A woman, aged 23, complained of vertigo, defective movements of the eyes and swaying to the right. Examination revealed paralysis of the left side of her face. There was complete paralysis of conjugate movements of the eyes to the left and slight paralysis of conjugate movements to the right, affecting especially the internal rectus. Convergence was preserved. Death resulted from tuberculous meningitis.

Necropsy revealed tuberculous meningitis of the base—a tubercle of the upper part of the pons projecting into the fourth ventricle, measuring 1.2 by 1 cm. It occupied the position of the two sixth nuclei and facial nerves as well as the posterior longitudinal fasciculi. There was ascending and descending degeneration of both posterior longitudinal fasciculi. The third nerve was normal.

Ewald: A man, aged 37, was tuberculous. The left eye would move neither out nor in; the right eye would move out but not in, in associated lateral movements. Closing the left eye made the abduction of the right eye more complete. Convergence was preserved. There were facial palsy of the left side and glycosuria.

Necropsy revealed a tubercle of the pons the size of a cherry stone. The specimen was turned over to Brasch for microscopic examination.

Group 7.—*Paralysis of lateral associated movements combined with paralysis of the elevators or depressors, from lesions in the neighborhood of the corpora quadrigemina.* Fourteen cases (Bárány, Kornilow, Leri and Perpére, Raymond

and Cestan,[117] Raymond and Claude, Raymond and Rose, Schoeler, Schoenherd, Spiller,[187] four, Uhthoff).

Bárány: A man, aged 39, who had cerebral syphilis, had crossed paresis of the right fifth and the left seventh nerves, later involving the right seventh. He was deaf in both ears, had difficulty in swallowing and speaking, and complete paralysis of the tongue; he was weak on the right side, hypesthetic and ataxic and had retention of urine. He had ptosis of the right eyelid, later of his left. Conjugate movements to the sides were wanting. Very slow nystagmus developed on attempting to look to the sides or upward. The right eye was weakened in convergence and in upward movements. The weakness of associated movements became paralysis, and the nystagmus was lost. Bilateral ophthalmoplegia developed. Reflex conjugate lateral movements were preserved and on vestibular stimulation conjugate deviation was obtained instead of the normal nystagmus.

Necropsy revealed syphilitic infiltration of the corpora quadrigemina extending down into the pons.

Raymond and Cestan: In a man, aged 43, a week after a violent emotional disturbance speech became thick and weakness developed on the left side. He had diplopia on looking to the side. Examination revealed paralysis of the left arm and leg and of the lower half of the left side of the face, with exaggerated reflexes and intention tremor. There was moderate hypesthesia, especially in the distal parts and paralysis of associated movements of the eyes to both sides, and diminished power of elevating the eyes. Nystagmus was present. The condition remained unchanged for ten years.

Multiple areas of sclerosis involving the left pyramidal tract and the right posterior columns of the cord at different levels were found. Other areas centered about the aqueduct of Sylvius and enclosed the third nuclei but did not destroy them. Other smaller areas were found in the pons.

Spiller: A man, aged 31, had been paretic in the right extermities and in both sides of the face, especially the left, for nine months. The muscles of mastication were weak. There were fibrillary tremors of the left masseter muscle and of the right side of the tongue. Tendon reflexes were exaggerated in the right extremities, and there was moderate wasting of the muscles. There was paresis of associated movements of the eyes upward and to the left. Bulbar speech, impaired hearing on the left, anesthesia of the left cornea and optic neuritis were present.

Necropsy revealed a large tubercle involving almost the entire left side of the pons and invading a little of the right half, extending into the lower portion of the cerebral peduncle. Most of the nerve cells of the left oculomotor nucleus were displaced. The left third nerve was normal. The left sixth and the spinal root of the fifth were much degenerated, and the left seventh and the motor root of the fifth were partially degenerated. The left pyramid was invaded. The aqueduct of Sylvius was much compressed from the left side.

GROUP 8.—*Paralysis of the abducens and of the oculomotor branches that should not come under the classification of paralyses of associated lateral movements of the eyeballs;* three cases.

Senator: A man, aged 52, had an apoplectic stroke, and later headache and mental dulness; he was paralyzed on the left side. Speech was disturbed. He was alcoholic. Twice a year he had attacks of confusion and vomiting, with hot and cold flashes. Examination showed that his left leg was weak, and he had a tendency to fall to the left. Walking quickly made him dizzy. There was incomplete ptosis on the left. Movements of the left eye were limited in all directions. The right eye was limited in abduction in both monocular and

binocular tests. The right pupil was smaller; both reacted slightly. Convergence was preserved, but to a subnormal extent. There was left facial palsy. The left side of the tongue was atrophic, protuded to the left and showed fine fibrilliary twitchings. There was anesthesia of the left half of the face, and paresis of the abductor of the left vocal cord. The knee reflexes were absent. Romberg's sign was positive.

Necropsy revealed an area of softening ventrolateral to the sixth nucleus, still within the tegmentum of the pons, but involving neither the left sixth nucleus nor the posterior longitudinal bundle (Marburg).

Uhthoff: A man, aged 45, had paralysis of both internal recti for lateral movements and for convergence. He had nystagmus. The patellar reflexes were increased. There was weakness of the left leg with ataxia. He had slight dementia.

Necropsy examination was not made. Diagnosis: Multiple sclerosis.

Bárány's case might be considered here.

I have recently observed a case of tuberculous meningitis with eye symptoms like those of Senator's patient, a spurious paralysis.

Group 9.—*Paralyses of associated movements of the eyes from lesions outside of the pons.* Six cases (Prévost, Urbantschitsch, Panas, Cushing[20]).

Prévost: The patient had paresis of the entire right side of the face and weakness of the right extremities. The eyes deviated to the left and could not be moved beyond the median line. There was diplopia on looking to the right.

Necropsy examination revealed a tumor the size of a hen's egg in the right cerebellar hemisphere.

Urbantschitsch: A girl, aged 8, had otitis media several weeks followed by partial recovery. One day she complained of headache, vomiting and pain in the neck. She was very sick. The right pupil was dilated. There was no Kernig's sign. She could not move her eyes to the left. A tache cerebrale was obtained. The pulse rate was 64, temperature normal. Examination of the left ear showed signs of recent inflammation and a polyp. The hearing was gone. At operation the mastoid antrum was found filled with inspissated pus. The patient died.

Necropsy revealed chronic otitis media in direct proximity to the left cerebellar hemisphere and in the hemisphere itself a destructive abscess the size of a hen's egg. There was no meningitis.

Panas: The patient had a progressive loss of sight for four years, with inability to move the eyes separately or conjugately in the lateral plane. Vertical movements were retained. There was spasm of the right arm and leg.

Necropsy revealed gray softening of the whole cortical layer of the left lobe of the cerebellum. The gray matter of the inferior vermis was the seat of a certain degree of softening. The cerebrum and brain-stem were healthy.

Gaussel thinks this may have been a case of compression. It is possible a minute lesion was overlooked for the symptoms are typical of a lesion involving both posterior longitudinal fasciculi.

Cushing: A woman, aged 37, complained at first of unsteadiness of gait, thickness of speech, immobility of the face and drooling at the corners of the mouth. There was numbness in the tongue. She was deaf on the left side. There was paresis of the left abducens. She was weak and showed loss of emotional control. She had severe headaches, vomiting, suboccipital discomforts and failing vision. The sense of smell and of taste became defective. Her mouth and lips were anesthetic. She had paresthesias of the left arm and it was

ataxic. She staggered when she walked, showed a positive Romberg sign and nystagmus.

There was some fluctuation of symptoms from time to time, but three years later she had lost vision, hearing, sense of smell and sense of taste. Practically all the cranial nerves were involved: First nerve, anosmia; second, blindness; third, almost complete ophthalmoplegia, conjugate deviation possible only to the right, then with nystagmus; fifth, areflexia cornealis, hypesthesia, hypalgesia and bilateral paralysis of muscles of mastication; seventh, almost complete paralysis of both sides of the face; eighth, bilateral tinnitus preceding deafness—no labyrinthine response; ninth and tenth, ageusia, dysarthria, dysphagia; eleventh, and twelfth, uninvolved, tongue in midline. Thus ten of the twelve pairs of cranial nerves were paralyzed. The woman died suddenly. Necropsy revealed a very large acoustic tumor springing from the left side.

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# CHEMICAL INVESTIGATIONS OF THE CENTRAL NERVOUS SYSTEM UNDER NORMAL AND PATHOLOGIC CONDITIONS

## CHEMICAL EXAMINATION OF THE CENTRAL NERVOUS SYSTEM IN TWO CASES OF GENERAL PARALYSIS

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### INTRODUCTION

For a study of the chemical changes in the central nervous system in pathologic conditions, general paralysis was chosen because these cases show, both macroscopically and microscopically, perhaps the greatest amount of change and a chemical examination should, therefore, indicate the greatest variation from normal, if such variations can be demonstrated by chemical methods.

Data dealing with the influence or effect of disease on the chemical constituents of the nervous system are still very meager. None of the older investigators made any attempts at a quantitative study of changes in the chemical composition of nerve tissue under pathologic conditions except to determine the percentage of water and very often also the total amount of phosphorus. That much of the earlier work on the chemistry of pathologic nerve tissue is so incomplete was due to a lack of knowledge of the substances to be estimated so that a more accurate comparative study of normal and pathologic material could be made. Following Thudichum's [1] extensive studies of the different constituents in the brain a new interest was awakened in the chemical study of the nervous system. We can, however, mention only two of the more recent methods which in any way permit us to make a more systematic quantitative chemical study of the nervous system under normal and pathologic conditions. These are the methods of Siegmund Fraenkel [2] and Waldemar Koch.[3] A brief description of these methods follows:

### METHODS

The method of Fraenkel consists in the study of the fat-like substances known as lipoids, separating these from one another by taking advantage of the fact that certain lipoids are more readily soluble in some of the fat solvents than in others. By successively extracting brain tissue with acetone, petroleum-

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2. Fraenkel, S.: Gehirnchemie, Ergebn. d. Physiologie, 1909, vol. 8.

3. Koch, W.: Methods for the Quantitative Chemical Analysis of Animal Tissue, J. Am. Chem. Soc. **31**:1329, 1909.

ether, benzol, alcohol and ether, different lipoid groups were removed, leaving behind a protein residue. These different lipoid groups are classified under the different solvents used for their extraction. This method has been developed and extensively used by Fraenkel and his associates for the study of brain tissue. Recently Pighini [4] and his co-workers have employed this method with some success for the study of chemical changes in the whole brain in a number of cases of general paralysis.

The method of Koch consists in the study of the three large chemical fractions or groups: proteins, extractives and lipoids. By first extracting the fresh brain material with 85 per cent. alcohol and with water, the extractives and lipoids are removed, leaving behind a protein residue. The lipoids are then separated from the extractives by precipitating the former in a watery emulsion of the total extract, with chloroform in the presence of acid (hydrochloric). The individual lipoids are then determined either directly or by calculation from some element or chemical radical characteristic of each individual lipoid. In each of these three main groups the elements sulphur, phosphorus and nitrogen are determined. W. Koch employed and developed this method for the study of the mammalian nervous system during its growth and development (in man [5] and in the Albino rat [6]), also for the study of the adult brain in certain forms of insanity.[7] This method was employed for the investigation reported in this paper. (An explanation of the different groups is given on page 222).

Besides these two methods there are still two others which, while not representing as complete an analysis, have been applied to the chemical study of the brain in general paralysis, and should therefore be mentioned here.

The one is the method of Smith and Mair,[8] which consists in fixing brain material in formaldehyd, drying at 37 C. to constant weight, then extracting with chloroform and further separating different lipoids by saponifying the extract with hot acetone and then determining these directly. By this method the total extract appears low, as compared with the total extract of Fraenkel and of Koch. A comparative study of changes in pathologic nerve tissue by this method with that of the other methods is thereby limited.

Another method is that of Nelson [9] which follows the general plan employed by W. Koch, that is, dividing nerve tissue into three large fractions or groups: proteins, extractives and lipoids. It differs from Koch's method, however, in

4. Pighini, G.: Chemische u. biochemische Untersuchungen ueber das Nervensystem unter normalen u. pathologischen Bedingungen. IV. Beitrag zur chemischen Zusammensetzung des Gehirns bei der progressiven Paralyse (Carbone, D., und Pighini, G.), Biochem Ztschr. **46**:450, 1912.

5. Koch, W., and Mann, S. A.: A Comparison of the Chemical Composition of Three Human Brains at Different Ages, J. Physiol. **36**:1, 1907.

6. Koch, W., and Koch, M. L.: Contributions to the Chemical Differentiation of the Central Nervous System. III. The Chemical Differentiation of the Brain of the Albino Rat During Growth, J. Biol. Chem. **15**:423, 1913.

7. Koch, W., and Mann, S. A.: A Chemical Study of the Brain in Healthy and Diseased Conditions with Especial Reference to Dementia Praecox, Arch. Neurol. & Psychiat. **4**:174, 1909.

8. Smith, J. L., and Mair, W.: On a Method of Quantitative Analysis of Tissue Lipoids with a Preliminary Note on Degeneration in the Brain, J. Path. & Bacteriol. **16**:131, 1911.

9. Nelson, Bert E.: Chemical Studies on the Central Nervous System, Psychiat. Bull. of the New York State Hospitals **9**:368, 1916.

that the further separation of the extract into lipoids and extractives is carried out by refrigerating the extract fraction at 0 C. when the lipoids separate out, leaving the extractives in solution. Nelson does not determine individual lipoids. In each of the three main groups the elements sulphur, phosphorus and nitrogen are also determined. Nelson determined nucleic acid, protagon and neurokeratin.

A comparison of these four methods indicates that the underlying principle is, generally speaking, similar; that is, each method aims to extract the lipoids from nerve tissue by means of fat solvents, leaving behind a protein residue. The solvents used and the technic employed for the separation and determination of the individual lipoids differs in each of these methods, however, and for greater detail and a clearer understanding of these methods the original articles should be consulted.

The extractives, or water soluble fraction, determined by W. Koch and also by Nelson have been almost entirely ignored by other investigators or only indirectly determined by Fraenkel. In normal adult nerve tissue this fraction is found to be constant, standing in a definite relation to the other chemical groups in the whole brain, as well as being definite in amount in each of the parts of the central nervous system studied. In view of this fact and because it is in this fraction that the intermediary and end products of nerve tissue metabolism are to be found, we feel justified in paying particular attention to this group.

The study of the distribution of the elements sulphur, phosphorus and nitrogen in nerve tissue has also received little attention. By studying the variations in the distribution of these elements in the three main groups we hope to show additional changes which have occurred under pathologic conditions, but which cannot otherwise be detected at the present time. These elements represent certain compounds in nerve tissue for which no quantitative determination has been made as yet.[10]

The chemical investigations of the nervous system in general paralysis have thus far been confined by different investigators to the whole brain. In the present investigation the analyses of an entire cerebral hemiphere (cerebrum[11]), corpus callosum, cortex, cerebellum and spinal cord in two cases of general paralysis are recorded. The object of analyzing the different parts of the central nervous system in general paralysis was to determine whether in this disease any special part of the brain undergoes greater changes than other parts.

## SUBSTANCES IN THE NERVOUS SYSTEM

Our present knowledge permits us to refer to only certain groups of substances in the nervous system which may be arranged under the following general headings

1. Water.
2. Proteins: neurokeratin, nucleoproteins, globulins.

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10. The lipoid-phosphorus has been used for the calculation of the "phosphatides" and the lipoid-sulphur for the calculation of the "sulphatides."

11. The analysis of the "cerebrum" represents an analysis of one entire cerebral hemisphere while that of the cortex and corpus callosum represents an analysis of the gray and white matter collected from the other hemisphere.

3. Lipoids: cholesterol, phosphatides, cerebrosides, sulphatides.

4. Extractives: organic extractives such as the nonprotein nitrogen substances, neutral-sulphur, etc., and inorganic salts, ash.

The chemical constituents of the normal adult human brain [11a] consist of: (1) water, 77 per cent.; the solids, which consist of (2) proteins, that is, the residue from alcohol and water extraction; (3) lipoids, alcohol-soluble and water insoluble, and (4) extractives, alcohol and water soluble. The lipoids are further subdivided into three groups: (*a*) cholesterol, (*b*) unsaturated lipoids (phosphatids), and (*c*) saturated lipoids (cerebrosids and sulphatids). These groups represent the different chemical constituents in nerve tissue as adopted by W. Koch and in the main also by Fraenkel and are the groups used in this study to determine the chemical changes in the central nervous system in general paralysis. The second and third groups are colloidal in nature, and the fourth group is in the main noncolloidal.

The properties of these constituents or groups are in brief as follows:

*Water.*—This is the most abundant element of protoplasm and has the property, so important for the cell, of accelerating all kinds of chemical reactions. In nerve tissue the percentage of water is an index of age as well as being definite in amount in different parts of the normal adult nervous system. A change in water content may therefore be looked on as an index of chemical changes in the tissues, and if increased above normal in the adult, it usually indicates a pathologic condition.

*Proteins.*—These make up about 38 per cent. of the solids. It is not possible to tell at the present time to what extent these are involved in the chemical activities of the nervous system as they have been too little studied. As a group, however, their decrease is an index of age. They are definite in amount in different parts of the normal adult nervous system.

*Lipoids.*—These make up about 54 per cent. of the solids. When one considers that under normal conditions the brain is one of the tissues richest in these fat-like substances, it is possible to think of the brain as having an active lipoid metabolism, especially when one considers that almost one half of these lipoids consist of unsaturated lipoids (phosphatids). Under normal conditions these phosphatids are probably in a state of unstable chemical equilibrium constantly breaking down and constantly being built up again. They are capable of auto-oxidation and when oxidized have a greater affinity for water

11 a. A more detailed description of the chemistry, anatomic distribution and physiologic significance of these different groups is given in the article by W. Koch and M. L. Koch referred to in footnote 6.

than when unoxidized (Mathews [12]). The saturated lipoids (cerebrosids and sulphatids), according to Mathews, have this same property of taking up water or combining with it, although possibly to a less extent. This is not true of cholesterol, however. (Besides these lipoids there are others less well defined; however, these are present only in small amounts which need not be considered in connection with this study.)

In nerve tissue the lipoids probably play an important rôle in conditioning the physical state of protoplasm. They are said to be in physical-chemical equilibrium with the proteins and with each other. According to Mathews,[13] and others, the function of the phosphatids is undoubtedly to produce with cholesterol the peculiar semifluid, semisolid state of protoplasm.

*Extractives.*—These make up about 8 per cent. of the solids. These represent the water-soluble constituents which include intermediary oxidation products and the larger part of the inorganic salts. The rôle played by these water-soluble extractives is probably very important in the chemical reactions of protoplasm. According to W. Koch,[6] this group as a whole is a rough index of the amount of metabolic activity going on in the tissues, as it represents at the same time the end-products of chemical activity as well as the culture mediums from which the more complex combinations are built up. In regard to this group Mathews [14] says: "It is very difficult to know whether these substances are normal constituents of the living brain, or whether they are formed by the hydrolytic decompositions which begin as soon as the circulation of the brain is interrupted." He believes, however, that "they pre-exist in the brain and that their accumulation there after death is due to the persistence of the vital processes in the absence of blood supply to remove the waste products. This view is supported by the relatively slight autolytic decomposition which brain material shows." [15]

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12. Mathews, A. P.: Physiological Chemistry, Ed. 2, New York, William Wood & Co., 1916, p. 98.

13. Mathews, A. P.: Physiological Chemistry, p. 88.

14. Mathews, A. P.: Physiological Chemistry, p. 579.

15. From a comparative chemical study on brains collected from one to thirty hours after death (kept in cold chamber), W. Koch concluded that the variations found are of little significance. He says, "The results are in harmony with other observations which indicate a very slow rate of autolysis in the brain. Nevertheless the material should be collected within twenty-four hours after death if possible."

A comparison of the chemical composition of brains from Albino rats dying during the night and of whom a necropsy examination was made the next morning, with brains from freshly killed (chloroformed) Albino rats of whom a necropsy examination was made immediately, showed no differences except those which could be attributed to differences in the age of the animals. The conclusion is therefore drawn that autolytic decomposition plays little, if any, part in influencing the chemical composition of the extractives.

Very few of these brain extractives have been isolated or identified as yet. The organic extractive group contains the nonprotein nitrogen substances, such as urea, amino acids, ammonia and creatinin, also the neutral sulphur. The inorganic salts consist largely of sodium, potassium, calcium, magnesium, chlorid, sulphate and phosphate. Some of these have been studied by W. Koch,[16] and more recently Clowes [17] has pointed out that the inorganic salts or "electrolytes" appear to play an extremely important rôle in conditioning the form and structure and in maintaining the equilibrium of the complex colloidal system which is designated as living protoplasm. The principal reason for reporting this group at the present time is to determine the ratio between these noncolloidal water-soluble constituents and the colloidal constituents (proteins and lipoids) in nerve tissue.

In general, we find, therefore, that we are dealing with group reactions in which the proteins and lipoids are classed as colloidal and have possibly a structural value while the extractives or noncolloidals represent the circulating material in the cell.

## PRESENTATION OF CHEMICAL DATA

The two cases chosen for this study were those in which clinical diagnosis of general paralysis was given (for case histories see end of paper).[18] The results of the chemical analyses of these two cases are summarized in Tables 1, 2, 3, 4 and 5.[19]

16. Koch, W.: Die Bedeutung der Phosphatide (Lecithane) für die lebende Zelle. II. Mitteilung, Ztschr. f. phys. Chemie **63**:432, 1909. Koch, W., and Pike, F. H.: Pharmacological Studies of the Phosphatides, J. Pharm. & Exper. Therap. **2**:245, 1910. Koch, W., and Williams, A. W.: Ibid., p. 251.

17. Clowes, G. H. A.: Antagonistic Electrolyte Effects in Physical and Biological Systems, Science **43**:750, 1916.

18. For controls are given two normal cases of cerebrum and cerebellum and four normal cases of spinal cord, all of which were recently analyzed by myself (Koch, M. L., and Voegtlin, C.: Hygienic Lab. Bull. No. 103, 1916, p. 51). The figures for the normal corpus callosum and normal cortex are from analyses made by W. Koch, published in connection with his chemical studies on the central nervous system.

19. In making a comparison between the values reported in the tables a definite plan has been followed. The values of normal cases are used as a standard with which the values obtained in general paralysis are compared. The *percentage difference* between the observed percentage values has been determined in each instance and the interpretation of the findings are based on these.

Values which vary from the normal by less than 10 per cent. are considered normal or said to show a tendency either to increase or decrease. Values varying from 10 to 20 per cent. are considered to be slightly different—slightly increased or slightly decreased. Those varying from 20 to 30 per cent. are considered to be different—increased or decreased. Those varying above 30 per cent. are considered to be greatly increased or greatly decreased. (The distinctions noted have been carefully maintained in interpreting the figures in the tables.)

TABLE 1.—Comparison of the Cerebrum, Cerebellum and Spinal Cord in Normal Persons with Those of Two Patients With General Paralysis (Koch)

| | Relative Proportions of Constituents in Percentage of Solids | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Cerebrum | | | | | Cerebellum | | | | | Spinal Cord | | | | | | |
| | Normal* | | | General Paralysis | | Normal* | | | General Paralysis | | Normal* | | | | | General Paralysis | |
| | | | | I | II | | | | I | II | | | | | | I | II |
| | | | Aver. | | | | | Aver. | | | | | | | Aver. | | |
| 1. Percentage of water | 77.1 | 76.6 | 76.9 | 77.82 | 79.19 | 78.60 | 77.66 | 78.13 | 78.18 | 77.26 | 70.34 | 71.46 | 71.16 | 73.43 | 71.60 | 72.66 | 72.09 |
| Percentage of solids | 22.9 | 23.4 | 23.1 | 22.18 | 20.81 | 21.40 | 22.34 | 21.87 | 21.82 | 22.74 | 29.66 | 28.55 | 28.84 | 26.57 | 28.40 | 27.34 | 27.91 |
| 2. Protein residue | 37.63 | 37.90 | 37.76 | 38.48 | 37.93 | 40.04 | 40.67 | 40.35 | 42.73 | 44.10 | 29.00 | 30.56 | 28.17 | 30.60 | 29.60 | 30.87 | 35.12 |
| Extractives | 7.98 | 7.76 | 7.87 | 14.52 | 15.22 | 10.41 | 7.04 | 8.72 | 11.46 | 14.98 | 5.70 | 5.61 | 5.77 | 5.24 | 5.60 | 6.46 | 9.035 |
| Lipoids | 54.39 | 54.34 | 54.37 | 47.00 | 46.85 | 49.55 | 52.29 | 50.92 | 45.81 | 40.92 | 65.30 | 63.83 | 66.06 | 64.16 | 64.80 | 62.67 | 55.85 |
| 3. (a) Cholesterol | 10.93 | 9.34 | 10.03 | 8.71 | 8.504 | 7.23 | 5.60 | 6.41 | 7.19 | 7.987 | 11.64 | 12.84 | 10.12 | 12.58 | 11.79 | 15.08 | 13.58 |
| (b) Phosphatids | 28.54 | 28.13 | 28.33 | 22.74 | 25.33 | 25.64 | 24.33 | 24.98 | 23.76 | 22.85 | 27.45 | 29.80 | 31.80 | 31.13 | 30.05 | 30.96 | 28.15 |
| (c) Cerebrosids | 7.25 | 6.04 | 6.64 | 7.38 | 8.57 | 9.41 | 5.34 | 7.37 | 7.22 | 6.63 | 11.57 | 12.38 | ..... | 11.80 | 11.91 | 12.22 | |
| | | | | | | 8.27 | 9.70 | 8.98 | 5.35 | 6.59 | 12.60 | 11.27 | 13.40 | 12.11 | 12.34 | 9.66 | 8.96 |
| Sulphatids | 9.73 | 9.58 | 9.65 | 9.43 | 11.78 | | | | | | | | | | | | |

* Koch, M. L., and Voegtlin, C.: Footnote 18.

TABLE 2.—Comparison of Normal Corpus Callosum (Five Cases) and Cortex (Three Cases) With Two Cases of General Paralysis (Koch)

| | | Relative Proportion of Constituents in Corpus Callosum (White Matter) | | | | | | | | Percentage of Solids Cortex (Gray Matter) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Normal† | | | | | | General Paralysis | | Normal† | | | | General Paralysis | |
| | | (a) | (b) | (c) | (d) | (e) | Aver. | I | II | (a) | (c) | (d) | Aver. | 1 | II |
| 1. | Percentage of water | 68.0 | 70.0 | ..... | 69.70 | 70.31 | 69.50 | 72.38 | 70.99 | 82.0 | .... | 83.2 | 82.6 | 84.10 | 82.20 |
| | Percentage of solids | 32.0 | 30.0 | ..... | 30.30 | 29.69 | 30.50 | 27.62 | 29.01 | 18.0 | .... | 16.8 | 17.4 | 15.90 | 17.80 |
| 2. | Protein residue | 29.96 | 28.10 | 28.70 | 27.1 | 29.25 | 28.62 | 30.42 | 30.29 | 46.6 | 45.7 | 47.1 | 46.4 | 49.38 | 52.50 |
| | Extractives | 4.75 | 5.80 | 6.10 | 6.30 | 5.12 | 5.61 | 7.07 | 7.464 | (8.8) | 13.2 | 15.4 | 14.3 | 19.90 | 19.38 |
| | Lipoids | 65.29 | 66.10 | 65.2 | 66.5 | 65.63 | 65.64 | 62.51 | 62.25 | .... | 41.1 | 37.5 | 39.3 | 30.72 | 28.12 |
| 3. | (a) Cholesterol | 15.2* | ..... | ..... | 10.25* | ..... | 12.72 | 15.83 | 14.53 | 3.9* | .... | 4.9* | 4.4 | 5.26 | 3.724 |
| | (b) Phosphatids | 27.13 | (22.10) | 27.90 | 31.0 | 27.63 | 28.41 | 29.75 | 25.67 | 21.6 | 24.5 | 23.7 | 23.2 | 19.41 | 17.00 |
| | (c) Cerebrosids | 14.3 | 17.1 | 17.7 | 18.30 | ..... | 16.85 | 13.13 | 13.30 | 8.6 | 7.9 | 8.8 | 8.4 | (2.55)* | (2.88)* |
| | Sulphatids | 4.37 | 7.30 | 4.7 | 8.65 | 7.46 | 6.50 | 12.66 | 10.91 | 8.0 | (....) | (....) | 8.0 | 3.50 | 3.40 |

* By difference. † Koch, W.: Footnote 18.

The figures given in Table 3 represent the percentage variation from normal, that is, the percentage value of the difference between the several observed percentages in Tables 1 and 2.

TABLE 3.—Deviations of Percentages in Brains of Patients With General Paralysis Based on Tables 1 and 2

| | | Water | | Proteins | | Extractives | | Lipoids | |
|---|---|---|---|---|---|---|---|---|---|
| | | Case I | Case II | Case I | Case II | Case I | Case II | Case I | Case II |
| 1 and 2 | Cerebrum | + 1 | + 3 | + 2 | 0 | +84 | +93 | −13 | −14 |
| | Cortex | + 1 | 0 | + 7 | +13 | +39 | +35 | −21 | −28 |
| | Corpus callosum | + 4 | + 2 | + 6 | + 5 | +26 | +33 | − 5 | − 5 |
| | Cerebellum | 0 | 0 | + 3 | + 8 | +31 | +74 | −12 | −19 |
| | Spinal cord | 0 | 0 | + 4 | +18 | +15 | +61 | − 2 | −13 |
| | | Cholesterol | | Phosphatids | | Cerebrosids | | Sulphatids | |
| | | Case I | Case II | Case I | Case II | Case I | Case II | Case I | Case II |
| 3 | Cerebrum | −13 | −15 | −12 | −10 | +11 | +29 | − 2 | +22 |
| | Cortex | +24 | −15 | −16 | −26 | .... | .... | −56 | −57 |
| | Corpus callosum | +20 | +22 | + 4 | −10 | −20 | −18 | +94 | +67 |
| | Cerebellum | +12 | +24 | − 5 | − 9 | − 2 | −10 | −40 | −26 |
| | Spinal cord | +27 | +15 | + 3 | − 9 | + 2 | .... | −21 | −27 |

1.[20] Water is normal or shows a tendency to increase. This increase in water is accompanied by a proportionate decrease in solids.

2. Proteins, that is, residue from alcohol and water extraction, were practically normal or showed only a tendency to increase.

Extractives, alcohol and water soluble, are greatly increased; the most pronounced change is in the cerebrum in both cases.

Lipoids, alcohol soluble and water insoluble, are either slightly decreased or decreased in all five parts in both cases; the most pronounced in the cortex; the least pronounced in the corpus callosum where these show only a tendency to decrease.

3. (*a*) Cholesterol appears to be increased in all parts except in the cerebrum, where it is slightly decreased. Percentage variations of cholesterol in the corpus callosum and cortex are not strictly comparable since this was not determined directly in the normal person.

20. These numbers refer to numbers in the tables which indicate different divisions into which the chemical groups have been divided in order to obtain a closer correlation between the chemical findings of the different investigators. For example, division 1 comprises water and solids; division 2, protein residue, extractives and lipoids; division 3, (*a*) cholesterol, (*b*) unsaturated lipoids (phosphatids), (*c*) saturated lipoids (cerebrosids and sulphatids); division 4, protein sulphur, lipoid sulphur, neutral sulphur, inorganic sulphur and total sulphur; division 5, protein phosphorus, lipoid phosphorus, extractive phosphorus and total phosphorus; and division 6, protein nitrogen, lipoid nitrogen, extractive nitrogen and total nitrogen.

(*b*) Phosphatids are slightly decreased in the cerebrum and in the cortex; in the other three parts these show a slight tendency to decrease.

(*c*) Cerebrosids are slightly increased in the cerebrum but in the corpus callosum they are slightly decreased. In the cerebellum and spinal cord these appear to be normal.

(Percentage variation of cerebrosids in the cortex could not be compared since these were not determined in these general paralytic brains.)

(*d*) Sulphatids are greatly increased in the corpus callosum; normal in the cerebrum of Case 1 and increased in the cerebrum of Case 2. The sulphatids in the other three parts were greatly decreased.

In Table 4 the distribution of sulphur, phosphorus and nitrogen calculated in percentage of total sulphur, total phosphorus and total nitrogen in the three chemical fractions (proteins, extractives and lipoids) is compared in the cerebrum, cerebellum and spinal cord. We find that in the protein fraction all three elements are practically normal —the sulphur and phosphorus showing only a tendency to increase (with the exception of the protein-phosphorus in the spinal cord of the patient in Case 1 in whom this is decreased), the nitrogen showing a tendency to decrease. In the lipoid fraction the sulphur is practically normal in the cerebrum, greatly decreased in the cerebellum and decreased in the spinal cord; the phosphorus and nitrogen are decreased in the three parts, mostly in the cerebrum. In the extractive fraction the neutral-sulphur is practically normal in the cerebrum, greatly increased in the cerebellum and possibly also in the spinal cord; the inorganic sulphur is normal in the cerebrum, greatly decreased in the cerebellum and greatly increased in the spinal cord; the extractive-phosphorus and extractive-nitrogen are greatly increased in all three parts. Total sulphur, total phosphorus and total nitrogen are practically normal.

In Table 5 the distribution of the elements sulphur and phosphorus in the corpus callosum and cortex are compared, calculated in percentage of total sulphur and total phosphorus (nitrogen had not been determined in the normal corpus callosum and cortex and could therefore not be compared here). Since the normal values for these two parts are obtained by older methods which are not altogether comparable with the methods in use at the present time, it is not possible to make a comparison with the same degree of confidence as was done in the other three parts. We can place most reliance on the figures for the lipoid phosphorus which we find to be greatly decreased in the cortex—even more than in the cerebrum—while this is little changed in the corpus callosum.

TABLE 4.—Comparison of Cerebrum, Cerebellum and Spinal Cord of Normal Persons With Those of Two Patients With General Paralysis (Koch)

| | Distribution of Sulphur, Phosphorus, and Nitrogen in Percentage of Total Sulphur, Total Phosphorus and Total Nitrogen | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Cerebrum | | | | | Cerebellum | | | | | Spinal Cord | | | | | | |
| | Normal* | | | General Paralysis | | Normal* | | | General Paralysis | | Normal* | | | | | General Paralysis | |
| | | | | I | II | | | | I | II | | | | | | I | II |
| | | | Aver. | | | | | Aver. | | | | | | | Aver. | | |
| 4. Protein sulphur | 59.30 | 58.20 | 58.74 | 62.02 | 60.23 | 61.10 | 60.64 | 60.87 | 71.27 | 65.40 | 47.20 | 42.38 | 46.60 | 42.63 | 44.70 | 49.65 | 51.04 |
| Lipoid sulphur | 30.04 | 31.01 | 30.53 | 27.11 | 29.05 | 28.62 | 29.22 | 28.92 | 17.89 | 18.40 | 42.87 | 43.82 | 43.30 | 46.65 | 44.16 | 37.50 | 29.08 |
| Neutral sulphur | 8.68 | 9.39 | 9.04 | 8.97 | 9.92 | 6.91 | 4.48 | 5.69 | 7.84 | 12.95 | 6.73 | 10.50 | 7.30 | 7.42 | 7.99 | (2.15) | 10.31 |
| Inorganic sulphur | 1.98 | 1.40 | 1.69 | 1.90 | 0.80 | 3.37 | 5.66 | 4.51 | 3.00 | 3.25 | 3.20 | 3.30 | 2.80 | 3.30 | 3.15 | 10.7 | 8.97 |
| Total sulphur (in per cent. of total solids) | 0.647 | 0.617 | 0.632 | 0.704 | 0.756 | 0.578 | 0.662 | 0.620 | 0.597 | 0.716 | 0.580 | 0.514 | 0.609 | 0.519 | 0.555 | 0.515 | 0 604 |
| 5. Protein phosphorus | 12.11 | 11.00 | 11.56 | 13.10 | 13.17 | 20.91 | 19.00 | 19.95 | 21.74 | 21.49 | 11.09 | 10.10 | 10.32 | 11.39 | 10.72 | 8.39 | 10.65 |
| Lipoid phosphorus | 74.96 | 75.16 | 75.06 | 64.40 | 67.50 | 67.84 | 66.50 | 67.17 | 61.01 | 56.60 | 82.06 | 83.20 | 85.33 | 82.45 | 83.26 | 82.56 | 77 62 |
| Extractive phosphorus | 12.93 | 13.84 | 13.38 | 22.47 | 19.32 | 11.25 | 14.50 | 12.87 | 17.25 | 21.91 | 6.85 | 6.70 | 4.35 | 6.17 | 6.02 | 9.05 | 11.71 |
| Total phosphorus (in per cent. of total sodids) | 1.44 | 1.45 | 1.45 | 1.37 | 1.456 | 1.46 | 1.42 | 1.44 | 1.511 | 1.56 | 1.30 | 1.39 | 1.45 | 1.43 | 1.39 | 1.44 | 1.467 |
| 6. Protein nitrogen | 80.00 | 79.53 | 79.78 | 76.96 | 74.30 | 80.83 | 80.32 | 80.58 | 80.45 | 80.20 | ..... | 75.34 | ..... | ..... | 75.34 | 73.24 | (75.56) |
| Lipoid nitrogen | 11.80 | 10.53 | 11.16 | 8.90 | 7.40 | 11.21 | 10.42 | 10.81 | 9.70 | 8.87 | ..... | 20.17 | ..... | ..... | 20.17 | 17.23 | (10.28) |
| Extractive nitrogen | 8.02 | 9.91 | 8.96 | 14.14 | 18.30 | 7.96 | 9.26 | 8.61 | 9.85 | 10.93 | ..... | 4.49 | ..... | ..... | 4.49 | 9.53 | (14.16) |
| Total nitrogen (in per cent. of total solids) | 7.097 | 7.180 | 7.44 | 7.16 | 8.69 | 8.407 | 7.764 | 8.085 | 7.74 | 8.09 | ..... | 6.81 | ..... | ..... | 6.81 | 6.31 | 6.91 |

* Koch, M. L., and Voegtlin, C.: Footnote 18.

TABLE 5.—Comparison of Normal Corpus Callosum (Three Cases) and Cortex (Two Cases) With Two Cases of General Paralysis (Koch)

| | Distribution of Sulphur and Phosphorus in Percentage of Total Sulphur and Total Phosphorus | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Corpus Callosum (White Matter) | | | | | | Cortex (Gray Matter) | | | | |
| | Normal† | | | | General Paralysis | | Normal† | | | General Paralysis | |
| | (d) | (f) | (e) | Aver. | I | II | (d) | (f) | Aver. | I | II |
| 4. Protein sulphur | 56.0 | 54.1 | 53.8 | 54.6 | 51.0 | 54.5 | 76.5 | 75.2 | 75.8 | 73.4 | 58.7‡ |
| Lipoid sulphur | 36.0 | 35.9 | 32.4 | 34.8 | 40.9 | 34.1 | 7.0 | 7.1 | 7.1 | 9.8 | 8.7 |
| Neutral sulphur | 5.0 | 6.5 | 7.5 | 6.3 | 6.3 | 9.3 | 10.0 | 12.2 | 11.1 | (16.8) | 26.8‡ |
| Inorganic sulphur | 3.0 | 3.5 | 6.2 | 4.2 | 1.8 | 2.1 | 6.5 | 5.5 | 6.0 | ( ) | 5.8 |
| Total sulphur (in per cent. of solids) | 0.50 | ... | 0.50 | 0.50 | 0.62 | 0.64 | 0.46 | ... | 0.46 | 0.71 | 0.78 |
| 5. Protein phosphorus | 5.0* | ..... | 12.4 | 12.4 | 10.6 | 12.3 | 5.0 | ..... | 5.0 | 17.1 | 19.4 |
| Lipoid phosphorus | 81.0* | ..... | 75.8 | 75.8 | 77.7 | 75.7 | 63.00 | ..... | 63.0 | 56.3 | 47.5 |
| Extractive phosphorus | 15.0* | ..... | 11.80 | 11.80 | 11.7 | 12.0 | 32.0 | ..... | 32.0 | 26.6 | 33.1 |
| Total phosphorus (in per cent. of solids) | 1.45 | ..... | 1.42 | 1.43 | 1.42 | 1.32 | 1.45 | ..... | 1.45 | 1.34 | 1.39 |

* Older method. ‡ Doubtful. † Koch, W.: Footnote 18.

The ratio of the protein sulphur to the neutral sulphur has been found to be a means of investigating protein metabolism in the central nervous system during its growth period.[21] In certain forms of mental disorder, this ratio was found changed in the cerebrum as indicated in Table 6.

In cases of dementia praecox for example this ratio was found to be greatly changed, due to the great decrease in the neutral sulphur. W. Koch reached the tentative conclusion that "in dementia praecox there exists a condition of metabolic deficiency." In pellagra a similar change was observed although less marked. It is therefore of interest to find that in general paralysis this ratio of protein sulphur to neutral sulphur is close to normal, which leads one to believe that changes in this disease point less toward a condition of "metabolic deficiency" and more toward a destruction of tissue as indicated by the decrease of the lipoid phosphorus and lipoid nitrogen.

TABLE 6.—RATIO OF PROTEIN SULPHUR TO NEUTRAL SULPHUR

| | Protein Sulphur | Neutral Sulphur |
|---|---|---|
| Normal (average of 5) | 58.8 | 8.9 |
| Dementia praecox* (average of 5) | 64.5 | 5.2 |
| Pellagra† (average of 5) | 65.5 | 7.2 |
| General paralysis (Case I) | 62.0 | 9.0 |
| General paralysis (Case II) | 60.2 | 9.9 |

* Koch, W.: Chemical Study of the Brain in Cases of Dementia Praecox, J. Exper. Med. 13: 301, 1911.

In summing up the chemical findings in the central nervous system in these two cases of general paralysis we find that the water and proteins tend to increase while the lipoids as a whole tend to decrease. The most marked change, however, is the great increase of the extractives in consequence of which the relative proportions of the lipoid group to the extractive group have been changed. To what extent these two groups have been changed in absolute differences between the percentages as found in Tables 1 and 2, for the different parts of these pathologic brains, is indicated in the following:

The lipoids in the different parts were thus decreased: In Case 1: cerebrum, 7.4 per cent.; cortex, 5.5 per cent.; cerebellum, 5.1 per cent.; corpus callosum, 3.3 per cent.; spinal cord, 2.1 per cent. In Case 2: Cerebellum, 10 per cent.; spinal cord, 9 per cent.; cortex, 8.1 per cent.; cerebrum, 7.6 per cent.; corpus callosum, 3.6 per cent. The extractives in these parts were thus increased: In Case 1: cerebrum, 6.6 per cent.; cortex, 3.3 per cent.; cerebellum, 2.8 per cent.; spinal cord, 0.9 per cent.; corpus callosum, 0.6 per cent. In Case 2: cerebrum,

21. Koch, W.: Footnote 5. Koch, M. L.: Footnote 6.

7.3 per cent.; cerebellum, 6.3 per cent.; spinal cord, 4.3 per cent.; cortex, 2.8 per cent.; corpus callosum, 2 per cent.

Of the individual lipoids the cholesterol is either normal or increased; the unsaturated lipoids (phosphatids) are decreased; and of the saturated lipoids the cerebrosids are practically normal in all parts except in the cerebrum, where they are increased and in the corpus callosum where they are decreased; the sulphatids are practically normal in the cerebrum and decreased in all parts except the corpus callosum where they are greatly increased.

The three elements, sulphur, phosphorus and nitrogen, follow in a general way the three main groups, as, for example, in the protein fraction all three elements are practically normal; in the lipoid fraction these are decreased, especially the phosphorus and nitrogen; while in the extractive fraction these same elements are greatly increased. It is of interest to note that the phosphorus and nitrogen throughout show greater changes than the sulphur in the parts of the central nervous system studied. The ratio of the protein sulphur to neutral sulphur in the cerebrum was found to be practically normal.

The cerebrum shows consistent percentage variation from normal for the different groups, especially in the relative proportion of the lipoids to the extractives. The cortex shows perhaps greater percentage variation from normal than the corpus callosum, especially for the total lipoids and the phosphatids. The cerebellum and spnial cord show generally less changes than the cortex but more pronounced changes than the corpus callosum. The corpus callosum is apparently least affected.

Whereas the two patients show the same relative changes in the different parts of the central nervous system, the patient in Case 2 almost without exception shows more intensive changes than the patient in Case 1.

W. Koch[7] some years ago determined different chemical constituents in the cortex and corpus callosum of one general paralytic brain and the sulphur and phosphorus distribution in the three main chemical groups of four general paralytic brains. From a comparison of these findings of W. Koch which were determined by an older method, with those reported in this paper, it is found that these are similar, except for the extractives in the cortex, which W. Koch stated are decreased. Since, however, the percentage variation from normal is not more than — 11, which is only a slight decrease, this may be considered practically normal. The decreased lipoid phosphorus with the corresponding increase of the extractive phosphorus in the whole brain is in agreement with my findings for the cerebrum (Tables 2 and 3).

TABLE 7.—Comparison of the Chemical Composition of the Cortex and Corpus Callosum of One Normal Person With Those of One Patient With General Paralysis (Koch and Mann, Older Method)

| | Relative Proportion of Constituents in Percentage of Solids | | | |
|---|---|---|---|---|
| | Cortex | | Corpus Callosum | |
| | Case 15 Normal | Case 16 G. P. | Case 15 Normal | Case 16 G. P. |
| 2. Proteins | 47.1 | 50.7 | 27.1 | 30.0 |
| Extractives* | 9.5 | 7.6 | 3.9 | 3.7 |
| Ash* | 5.9 \| 15.4 | 6.0 \| 13.6 | 2.4 \| 6.3 | 3.2 \| 6.9 |
| Lecithins and kephalins† | 23.7 | 23.9 | 31.0 | 25.0 |
| 3. Cerebrins‡ | 8.8 | 9.4 | 18.3 | 18.2 |

* Extractives. † Phosphatids. ‡ Cerebrosids.

TABLE 8.—Comparison of the Chemical Composition of the Brains of Two Normal Persons and Those of Four Patients With General Paralysis (Koch and Mann)

| | Distribution of Sulphur and Phosphorus in Percentage of Total Sulphur and of Total Phosphorus | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Normal | | General Paralysis | | | | Averages | |
| | Case 18 | Case 70 | Case 22 | Case 23 | Case 24 | Case 40 | Normal | General Paralysis |
| 4 | | | | | | | | |
| Protein sulphur | 60.9 | 62.6 | 56.7 | 57.1 | 62.0 | 61.4 | 61.7 | 59.3 |
| Lipoid sulphur | 28.6 | 25.9 | 30.2 | 30.8 | 25.1 | 28.4 | 27.2 | 28.6 |
| Neutral sulphur | 7.2 | 8.1 | 9.3 | 8.3 | 9.1 | 6.4 | 7.7 | 8.3 |
| Inorganic sulphur | 3.3 | 3.4 | .... | 3.7 | .... | .... | 3.4 | 3.7 |
| Total sulphur in percentage of total solids | .... | .... | .... | .... | .... | .... | 0.50 | 0.48 |
| 5 | | | | | | | | |
| Protein phosphorus | 3.9 | 5.7 | 5.9 | 4.8 | 4.6 | 4.6 | 4.8 | 5.0 |
| Lipoid phosphorus | 71.8 | 75.0 | 69.3 | 70.6 | 68.2 | 69.9 | 73.4 | 69.5 |
| Extractive phosphorus | 24.2 | 19.4 | 24.7 | 24.7 | 26.9 | 25.6 | 21.8 | 25.5 |
| Total phosphorus in percentage of total solids | .... | .... | .... | .... | .... | .... | 1.45 | 1.46 |

Other chemical studies on the whole brain in general paralysis by different investigators may now be considered. In 1912, Pighini[4] reported the chemical findings in five cases and in 1914 he, together with Barbieri,[22] reported seven additional cases of general paralysis, two of which they also studied histochemically. The main chemical changes in general paralysis, as found by these investigators (Table 9), are

22. Pighini, G., and Barbieri, P.: Chemische und histochemische Untersuchungen über die lipoiden Abbaustoffe des Gehirns bei progressiver Paralyse, Ztschr. f. d. ges. Neurol. u. Psychiat., Orig. **25**:353, 1914.

TABLE 9.—Comparison of the Brain in Two Normal Persons With Those of Twelve Patients With General Paralysis (Fraenkel Method) by Pighini and Barbieri

| | Relative Proportion of Constituents in Percentage of Solids | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 |
| | Normal | | Year of Analysis, 1912 | | | | | Year of Analysis, 1914 | | | | | | |
| | | | Age in Years | | | | | Age in Years | | | | | | |
| | | | N. S. 52 | L. C. 43 | M. C. 49 | E. B. 42 | M. B. 47 | G. S. 53 | A. F. 41 | L. B. 45 | C. Q. 37 | T. T. 31 | L. M. 42 | M. T. 40 |
| 1. Percentage of water | 77.0 | 76.10 | (83.0) | 77.81 | 84.58 | 78.97 | ..... | 80.83 | 78.88 | 82.77 | 82.29 | 79.80 | 77.91 | 77.20 |
| Percentage of solids | 23.0 | 23.90 | (17.0) | 22.19 | 15.42 | 21.03 | ..... | 19.17 | 21.12 | 17.23 | 19.71 | 20.20 | 22.09 | 22.80 |
| 2. Protein residue | 31.63 | 38.67 | ..... | 41.94 | ..... | ..... | ..... | 46.52 | 46.21 | 53.80 | 51.07 | 50.00 | 42.80 | 45.16 |
| Extractive (including leukopoiin, a phosphatid) | 9.64 | ..... | (4.5) | ..... | 8.97 | 6.00 | 11.84 | 4.90 | 4.30 | 3.32 | 4.67 | 6.46 | 6.05 | 8.99 |
| Lipoids | 58.73 | ..... | ..... | ..... | ..... | ..... | ..... | 48.58 | 49.49 | 42.88 | 44.26 | 43.34 | 51.15 | 45.55 |
| 3. Acetone extract* | 20.60 | 14.64 | (26.71) | 30.48 | 22.87 | 24.60 | 31.32 | 22.15 | 19.00 | 16.00 | 17.32 | 22.10 | 21.70 | 21.40 |
| (a) Cholesterol (crude) | 10.96 | ..... | (24.2) | ..... | 13.90 | 18.60 | 19.48 | 17.35 | 14.70 | 12.68 | 12.65 | 15.64 | 15.65 | 12.41 |
| (b) Unsaturated lipoids extracted with pertoleum-ether† | 27.836 | 28.85 | (14.28) | 12.33 | 23.14 | 13.93 | 11.23 | 17.76 | 25.50 | 20.03 | 13.45 | 15.39 | 26.40 | 18.16 |
| (c) Saturated lipoids | 20.70 | 17.84 | ..... | 15.25 | .... | ..... | ..... | 13.94 | 8.51 | 10.35 | 18.08 | 12.87 | 9.00 | 15.22 |
| Extracted with benzol | 13.53 | 12.27 | ..... | 6.20 | ..... | ..... | ..... | 9.03 | 5.55 | 6.00 | 14.58 | 9.37 | 2.09 | 11.49 |
| Extracted with alcohol | 6.258 | 4.46 | ..... | 8.75 | ..... | ..... | ..... | 3.68 | 2.46 | 4.35 | 3.50 | 3.13 | 6.80 | 3.73 |
| Extracted with ether | 0.92 | 1.11 | ..... | 0.30 | ..... | ..... | ..... | 0.23 | 0.50 | .... | .... | 0.37 | 0.11 | .... |

* Sum of cholesterol and extractives. † Phosphatid.

an increase in water, proteins and cholesterol and a decrease of the lipoids as a whole and the unsaturated lipoids (phosphatids) in particular, as well as the saturated lipoids (cerebrosids and sulphatids). The relative proportion of the different lipoid groups among themselves were reversed. As, for example, the acetone group consisting of cholesterol and extractives, was greatly increased in eight of the twelve cases so that this is now greater than the normally high petroleum-ether extract group, the latter representing the unsaturated lipoids. The other extracts—from benzol, alcohol and ether—representing the

TABLE 10.—Comparison of Three Normal Brains With Those of Three Patients With General Paralysis and Two Patients With Hemiplegia (Smith and Mair) *

| | 2 | 3 | | 5 |
|---|---|---|---|---|
| | Chloroform Extract Percentage of Dried Brain | Cholesterol in Percentage of Extract | Cerebrosids in Percentage of Extract | Phosphorus in Percentage of Extract |
| Normal: | | | | |
| Case 1 (peritonitis) | 46 | {22.0† {20.3 | {20.7† {20.2 | 1.58 |
| Case 2 (cerebral hemorrhage) | 42 | 21.8 | {20.4 {19.5 | 1.59 |
| Case 3‡ (cerebral thrombosis, normal area) | 51 | 21.4 | {18.1 {17.8 | 1.60 |
| General Paralysis: | | | | |
| Case 1 | 38 | 18.0 | 10.0 | 1.22 |
| Case 2 | .. | {20.2 {19.2 | {12.0 {10.0 | 1.34 |
| Case 3 | 43 | {20.0 {20.4 | {10.2 {11.5 | 1.31 |
| Hemiplegia (degenerated areas): | | | | |
| Case 1 (hemorrhage) 4 months' history | 51 | {41.0 {42.6 | { 8.0 {10.0 | 0.54 |
| Case 2 (thrombosis) 3 weeks' history | 43 | 29.6 | { 4.8 { 4.5 | 1.23 |

* The table was reconstructed to include only comparable data.

† "In this table the bracketed figures indicate two analyses of the same material, and they are given in this form in order to indicate the accuracy of the methods for cholesterol and cerebrosids respectively."

‡ "Normal No. 3 and hemiplegia No. 2 are from the same brain, the normal area being taken from the unaffected hemisphere."

saturated lipoids, varied among themselves although with less consistency. These findings indicate, according to Pighini and Barbieri, that while all twelve paralytic brains have undergone changes, brains may be affected differently. These findings are in agreement with those of the cerebrum in the two paralytic cases of this study.

Smith and Mair,[8] who analyzed three normal and three general paralytic brains (Table 10), also found a loss of lipoids (chloroform extract) in pathologic brains. In percentage of this chloroform extract they found the cerebrosids greatly decreased, the cholesterol normal and

the phosphorus, which represents the phosphatids, decreased. This is in agreement with our findings in the cerebrum with the exception of the great decrease of the cerebrosids. Two cases of hemiplegia are introduced in Table 10 for comparison.

Nelson [9] analyzed only one general paralytic brain (Table 11), and since he does not give any figures for the normal, the figures for the normal brain from Table 1 have been introduced in Table 11. In comparing Nelson's figures with these normal figures, one arrives at similar conclusions regarding changes in the brain in general paralysis. Nelson found water and proteins increased and the lipoids as a whole

TABLE 11.—Comparison of Normal Brain (Average of Two Cases, Koch) With One Case of General Paralysis (Nelson)

| | | Normal Analyst, M. L. Koch | General Paralysis Analyst, B. E. Nelson |
|---|---|---|---|
| 1. | Percentage of water | 76.9 | 81.7 |
| | Percentage of solids | 23.1 | 18.3 |
| | | In Percentage of Solids | In Percentage of Solids |
| 2. | Protein residue | 37.76 | 50.75 |
| | Extractives | 7.87 | 10.83 |
| | Lipoids* | 54.37 | 38.42 |
| 3. | Nucleic acids | ..... | 0.32 |
| | Protagon | ..... | 2.03 |
| | Neurokeratin | ..... | 5.00 |
| 4. | Protein sulphur | 0.372 | 0.683 |
| | Lipoid sulphur | 0.197 | 0.105 |
| | Extractive sulphur | 0.068 | 0.033 |
| | Total sulphur | 0.637 | 0.821 |
| 5. | Protein phosphorus | 0.154 | 0.285 |
| | Lipoid prosphorus | 1.065 | 0.613 |
| | Extractive phosphorus | 0.225 | 0.205 |
| | Total phosphorus | 1.44 | 2.10 |
| 6. | Protein nitrogen | 5.826 | 7.861 |
| | Lipoid nitrogen | 0.911 | 1.390 |
| | Extractive nitrogen | 0.701 | 2.550 |
| | Total nitrogen | 7.438 | 11.800 |

* Individual lipoids not determined.

decreased. The extractives, according to Nelson, appear to show little change which is constant, but which, when compared with the normal figures in the table, show the extractives to be considerably increased in this one case, which would be in agreement with our findings. According to Nelson, these changes seem to produce nearly proportional changes in the amounts of protein phosphorus and protein nitrogen, while protein sulphur is only relatively increased, which he attributes to increased amounts of neurokeratin; the lipoid phosphorus is greatly decreased and to a less extent the lipoid nitrogen and the lipoid sulphur; the extractive phosphorus is practically normal, the extractive nitrogen is quite strongly increased and the extractive sulphur to a less degree. Total sulphur, phosphorus and nitrogen appear to be increased.

## DISCUSSION

From the data presented it is found that there are certain general changes of the brain in general paralysis. These changes are found in the whole brain as well as in its parts, the cerebrum showing perhaps the most consistent change throughout, the cortex showing a greater percentage variation from normal than the corpus callosum; the cerebellum and the spinal cord show perhaps less change than the cortex, but more pronounced than the corpus callosum. These changes are a slight increase in water (moisture) in the fresh tissue and in the solids a relative increase of proteins and possibly also cholesterol and a decrease of the lipoids as a whole. Of the latter, the unsaturated lipoids (phosphatids) showed the most consistent change (decrease); the saturated lipoids (cerebrosids and sulphatids) showed less consistent changes although as a group they probably also decrease (Table 9). Since proteins and cholesterol are practically normal when calculated in percentage of fresh tissue, these are probably only increased in percentage of solids is so far as the lipoids have decreased.

In the present investigation, in addition to these changes, there was found a marked increase in the extractives (water-soluble substances consisting of organic extractives and inorganic salts). The lipoid phosphorus and lipoid nitrogen were decreased while the extractive phosphorus and the extractive nitrogen were increased (Koch and Nelson).

From earlier work on degenerative diseases of the nervous system, chemical evidence of the breakdown of nervous tissue was obtained by the discovery of certain disintegration products in the spinal fluid and in the blood of patients. The determination of phosphorus constitutes one of the first attempts to study changes under pathologic conditions. Halliburton [23] and his co-workers who studied "phosphatid degeneration" in nerve tissue, claim that the phosphatid portion of the molecule is freed or liberated, leaving behind the "fatty portion of the molecule" which, according to them, gives the Marchi reaction. Besides phosphorus, which Halliburton and his co-workers found decreased in the tissue and increased in the blood, they studied nitrogen (by the cholin radical) and found by both chemical and physiologic tests that this was also increased in the blood of experimental animals in whom the nerve had been cut and allowed to degenerate for a certain number of days.

It is therefore possible to think of the less stable lipoids (unsaturated lipoids or phosphatids) as breaking down from their physical or physical-chemical combinations with the proteins and with other lipoids, with a

23. Halliburton, W. D.: The Croonian Lectures on the Chemical Side of Nervous Activity, John Bale Sons and Danielson, Ltd., 1901.

subsequent appearance in the extractive fraction of some of the splitting products of simpler molecular composition. The decrease of the lipoid phosphorus and lipoid nitrogen fractions with the increase of the extractive phosphorus and extractive nitrogen fraction would indicate such a change.

Why cholesterol remains in the tissues or appears to be increased is not well understood. It has been suggested by Pighini and Barbieri that cholesterol acts as a protective agent in that it neutralizes the action of the syphilitic toxin. Since cholesterol, however, appears to be relatively inert chemically, its presence in the tissue is therefore probably only important to the cell from a physical or mechanical standpoint. It is present largely in the nerve sheaths to which it is supposed to add mechanical stability.

One would expect the saturated lipoids, which appear to be confined largely, although not entirely, to the white matter (corpus callosum) to correspond closely to this part of the nervous system or run more or less parallel to it in degree of change. This was found to be the case.

The chemical as well as the structural changes found in the brain of general paralysis are probably the result of autolytic processes. In cells undergoing autolysis, Wells[24] states that fat-like "myelin" droplets appear, and presumably represent cell lipoids set free through changes in the cell proteins. Wells goes on to say that these droplets "are characterized by staining with osmic acid but not with Sudan III, which shows them not to be simple fats or lipoids, but they are undoubtedy precursors of true fatty degeneration (Hess and Saxl[25]); they probably consist chiefly of lecithin (phosphatides) with more or less free fatty acids and relatively little cholesterol (Aschoff)."

Pighini and Barbieri have observed an increase of lipoid granules whenever the metabolism of the cell is slowed or in some way changed, as in senescence or with certain poisons or in certain diseases of the nervous system. To what extent we are justified in drawing conclusions from these observations on tissue degeneration has to be determined by a more thorough study of the different chemical constituents. It would seem, nevertheless, that the chemical picture obtained from our present studies of general paralysis is not unlike that of lipoid degeneration.

We should ask ourselves the question: Are these chemical changes observed in general paralysis typical of this disease or do they represent a general picture of nerve tissue degeneration? One might expect to find similar changes in a disease in which great or evidently acute

24. Wells, H. G.: Chemical Pathology, Philadelphia, W. B. Saunders Company, Ed. 3, 1918, Chapter 14.

25. Hess and Saxl: Virchows Arch. f. path. Anat. **202**:149, 1910.

destruction of nerve tissue has occurred. As far as we know, however, no other forms of mental disorder which have been studied chemically have shown such marked changes. Smith and Mair analyzed sections of degenerated areas of the brain in two cases of hemiplegia in which they found the cerebrosids decreased to an even greater extent than in general paralysis and the chloesterol more greatly increased. The phosphorus was also decreased. In dementia praecox, W. Koch found the brain practically normal except for the neutral sulphur fraction which in percentage of total sulphur was greatly diminished while the inorganic sulphur and protein sulphur were relatively increased. The nine cases examined by him, while varying among themselves, all tended in the same direction, namely, diminution of neutral sulphur. This variation appeared to be independent of the cause of death. Koch, therefore, concluded that it was not unreasonable to suppose that the subject of this mental disorder might possibly "possess a general bodily inherent deficiency for oxidation processes." In five cases of pellagra analyzed by myself a similar, although less marked, decrease of neutral sulphur was observed in the cerebrum with a tendency for this fraction to decrease in the spinal cord. Certain degenerative changes were also noticed in this disease although not as marked as in these general paralytic brains. No such marked change in the distribution of the sulphur was observed in general paralysis. On the other hand, the phosphorus and nitrogen fractions, which are more specifically identified with the structural elements of nerve tissue, have been changed, as indicated in the body of the paper.

## SUMMARY

Extensive chemical analyses of five parts of the central nervous system in two cases of uncomplicated general paralysis show the following changes as compared with normal controls:

1. A tendency for the water and proteins to increase and for the lipoids as a whole to decrease.

2. The extractives (water-soluble substances) are considerably increased, and, since the total solids have been very little changed, these probably compensate for the loss of the lipoids, especially the phosphatids.

3. Of the lipoids, cholesterol shows a relative increase in all parts except in the cerebrum where it may be considered to be practically normal. The phosphatids (unsaturated lipoids of Fraenkel) show a consistent decrease presumably due to a disturbance in the lipolytic processes associated with the degeneration of the tissue. The cerebrosids and sulphatids (saturated lipoids of Fraenkel) show less consistent changes. Since these are largely associated with the myelinated sheath (white matter), which showed less change on the whole in these

brains than the gray matter, these have probably been less affected; the lipoid phosphorus and lipoid nitrogen were decreased, while the extractive phosphorus and extractive nitrogen were increased.

4. Other chemical studies of nerve tissue (whole brain) in general paralysis check these findings: Pighini and Barbieri (Fraenkel method) observed in twelve cases of general paralysis an increase of water and proteins and a decrease in the total lipoids. The unsaturated lipoids were greatly decreased and the saturated lipoids, while decreased as a group, varied among themselves. Cholesterol was increased. Smith and Mair found in three cases of general paralysis a decrease of lipoids (chloroform extract), and in fractionation of this chloroform extract, a marked decrease of the cerebrosids, the cholesterol normal and the phosphorus decreased. Nelson, who analyzed only one general paralytic brain, found the water and proteins increased and the lipoids as a whole decreased. The extractives are probably increased. The lipoid phosphorus and lipoid nitrogen were decreased while the phosphorus and nitrogen in the extractive fraction were increased.

5. These changes in general paralysis present a chemical picture of lipoid dgeneration, where the water and water-soluble substances have increased at the expense of the lipoids, especially the phosphatids.

6. From a comparative study of different forms of insanity we find that general paralysis differs from dementia praecox, for example, in that the destructive changes in the former affect several constituents and not one constituent in particular, while in dementia praecox, W. Koch found an unmistakable decrease in the nonprotein neutral sulphur fraction in both the gray and white matter of the brain though the other constituents appeared practically normal.

7. The cerebrum in these general paralytic cases shows perhaps the most consistent change in the different chemical groups, especially in the relative proportion of the lipoids to the extractives. The cortex shows a greater percentage variation from normal than the corpus callosum; the cerebellum and spinal cord show perhaps less changes than the cortex but more pronounced than the corpus callosum. Least of all affected was the corpus callosum.

8. Whereas the two cases of general paralysis show the same relative changes in the different parts of the central nervous system, Case 2 almost without exception shows more changes than Case 1.

9. Until recently very little systematic work has been done on the quantitative separation of the chemical constituents of nerve tissue. Practically no work appears in the literature on chemical changes in pathologic nerve tissue. We find only four references to the chemical examination of the brain in general paralysis. The methods used for the chemical study of the brain are very different so that only a broad comparison of findings in general paralysis could be made. The method

of Fraenkel and W. Koch compared favorably. When the chemical findings of each investigator were compared with normals determined by the same method, we could arrive at certain general conclusions concerning changes in general paralysis. These have been mentioned.

## REPORT OF CASES

CASE 1.—*Clinical Summary.*—George G., admitted Oct. 13, 1913, aged 38, a bookkeeper, who is said always to have been of a shy, retiring nature, but who had apparently been efficient at his work, from his own account had had syphilis at the age of 18. He was married at the age of 29; there were no miscarriages or children. After marriage his wife and he ran a small store, but it is said that the patient never waited on customers, leaving this to his wife. At about the age of 33 he became nervous and irritable, made blunders to which he was indifferent, and at the age of 35 he ceased working entirely, became filthy in his habits, and had numerous dizzy spells. He was supported by his wife. He complained a great deal, finally, of the noises in the street, and of people in the house where he lived, and went to the police asking for a warrant for a baby who was crying on the floor above.

On admission to the Manhattan State Hospital, he was unusually quiet and cooperated to the best of his ability in the examination, but at times became rather apprehensive, saying the attendants wanted to kill him. There were no hallucinations and there was no grandiose trend. He had spoken, however, of suing the landlord for $50,000 for not repairing a stove, and saw nothing unusual in this idea. He knew he was in a hospital, but could not locate it. It was said that he identified those about him correctly and that his memory for the recent past was "fairly good," but his mind was not clear concerning details. He gave a varying account of his life, but there were many discrepancies in dates, which he did not realize. There were only a few mistakes in calculation, in which he had probably been efficient as a bookkeeper. He believed that there was nothing wrong with his mind, and he had no plans for the future.

*Examination.*—On admission the pupils were unequal and irregular and reacted to light and accommodation; the knee jerks were exaggerated; speech was characteristic of general paralysis; lumbar puncture showed 40 cells and positive globulin; a Wassermann test was not made.

*Course of Illness.*—During the early part of his hospital residence he was up and around the ward, but he gradually became weaker and ataxic, and for at least ten months before death he was confined continually to bed. Mental deterioration was also evidently progressive, and he finally became markedly deteriorated; practically no information could be obtained from him. He gradually became exhausted and died Oct. 18, 1915.

*Necropsy Examination.*—This was performed twelve hours postmortem by Dr. Clarence O. Cheney. The remains were those of a tall, much emaciated, poorly built man of about 40 with sacral decubitus. The brain weighed 1,135 gm., was small, and showed a striking atrophy of the frontal lobes, the convolutions being about half their normal thickness; the widened fissures were filled with opalescent fluid. Less marked, but still evident, atrophy was present in the temporal, parietal and occipital regions. The cerebellum was of good size, without definite atrophy. Microscopic examination demonstrated in all sections characteristic changes of general paralysis, with extensive and marked

thinning and disorganization of the cortex, in addition to the exudate in the pia, cortex and marrow of lymphoid and plasma cells. The neuroglia showed activity in the presence of large cell bodies containing pigment, and there was a good deal of pigment débris in the pia and along the cortical vessels. The vessels did not show syphilitic endarteritis, and there were no softenings.

The spinal cord was of good size, not appearing atrophic. The pia showed microscopically a moderate exudate of lymphoid and plasma cells, but this exudate was not evident in the substance of the cord. The anterior horn cells varied from normal to conditions of pigmentary degeneration, distortion and apparent atrophy, with a probable loss of cells in some places. No tract degenerations were evident.

Considering the previous bedridden condition of the patient, the appearance of the lungs was good, showing only a moderate purulent bronchitis and hypostatic congestion, without pneumonia. The aorta and other vessels were free from definite evidence of syphilitic involvement, and the other viscera showed no significant pathologic changes grossly or microscopically.

Case 2.—*Clinical Summary.*—Catherine E., admitted Dec. 16, 1913, aged 33, an Irish woman who was said to have been widowed but of whose early life nothing was known; admitted syphilis; at what age it was acquired is not known. No account was obtained of the onset of her trouble except that she had become confused and on April 7, 1913, was taken from the Salvation Army Home where she had been for two weeks.

*Examination and Course.*—She was admitted to Central Islip State Hospital on April 9, 1913, where she was still confused; she had a poor memory and made many contradictory statements. Her pupils were of the Argyll Robertson type. There were marked tremors; the knee jerks were absent; the Romberg sign was present, and the gait was unsteady. The Wassermann reaction in the spinal fluid was positive. After slight improvement she was discharged on July 25, 1913, to relatives in Pennsylvania. The diagnosis made was general paralysis.

The patient was admitted to the Manhattan State Hospital on Dec. 6, 1913, with no account of the interval. She was much disturbed and was very expansive, saying she was the Duchess of Denby, was going to marry King George, and had "loads of money." The physical signs were the same as at Central Islip. The spinal fluid showed a strongly positive globulin and 24 cells. The spinal fluid Wassermann test was not repeated.

During her residence she quieted down. She became bedridden as a result of ataxia, but she was good-natured, remained grandiose, and although she showed a poor memory for remote events, she was approximately oriented and her memory for events that happened in the ward was "quite fair." During her last year of residence she had two attacks of weakness. She recovered from the first after two weeks; the last began several days before death with gradual failure and a high temperature on the day before death. No physical signs were found to account for the temperature. She died, Jan. 27, 1916.

*Necropsy Examination.*—This was performed three hours postmortem by Dr. Clarence O. Cheney. The remains were those of a well built, muscular woman, appearing to be about 30 years of age; height, 5 feet 2 inches (157.5 cm.); weight estimated at 130 pounds (59 kg.), and emaciation was not noticeable. The brain weighed 1,015 gm., was small and showed marked atrophy, not only in the frontal regions, but also in the parietal and temporal regions. The atrophied tissue was sclerotic on palpation and on cutting. Microscopically

there were the characteristic changes of general paralysis, with much meningeal and deep perivascular exudate of lymphoid and plasma cells, and thinning and disorganization of the cortex. The changes were most marked in the frontal sections, but diagnostic alterations were evident in all other areas examined, including the occipital regions. A few cerebral medium-sized vessels showed evidence of syphilitic endarteritis, but no obliterations were found and no gross or microscopic softenings were evident.

The spinal cord was small throughout, this being considered out of proportion to the woman's development. The pia was chronically thickened and opaque. Microscopic examination of cervical, thoracic and lumbar sections showed a characteristic meningeal and deep perivascular exudate. The anterior horn cells appeared well preserved except for moderate granulation in some of them. Myelin sheath stains showed a degeneration of part of the deeper posterior column fibers, but there was no clean-cut tract degeneration.

Except for a moderate purulent bronchitis and hypostatic pulmonary congestion, gross and microscopic examination of the thoracic and abdominal viscera showed no significant pathologic changes. It was considered that the cerebral process had been the cause of death.

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# Abstracts from Current Literature

A CRITICAL REVIEW OF DECEREBRATE RIGIDITY. J. LHERMITTE, Ann. de méd. **10**:228, 1921.

Some of our present ideas concerning certain rigid states brought about by injury to the nervous system are discussed fully. The fact that increased activity of functions controlled by the nervous system is due to the absence of a part of the nervous system and is not due to irritation, is given particular emphasis. The exceptions to this rule, as illustrated by jacksonian epilepsy, are also discussed. Lhermitte emphasizes the fact that the manifestations of transections of the dorsal portions of the spinal cord as well as of those injuries whose residua are manifested by spasticity and hemiplegia, are due to the liberation of inferior integrations rather than to irritation. These are negative rather than positive pictures.

Lhermitte, after an introduction giving credit to Hughlings Jackson, Head and Kinnier Wilson for the development of the conception of decerebrate rigidity, proceeds to analyze the experimental data which leads up to Wilson's idea of the occurrence of decerebrate rigidity in man. Sherrington removed all parts of the nervous system except the spinal cord, medulla, pons, midbrain and peduncles in monkeys and dogs. As a result the animals when suspended assumed a constant and peculiar posture. The four legs were carried backward and were adducted. The elbow was extended while the wrist was flexed and the palm of the hand in the monkey was turned outward. The hind legs were in marked extension and carried backward. The tail no longer responded to the effect of gravity but was maintained horizontally and sometimes curved upward. The dorsolumbar vertebral column, as well as the neck, was rigid and in a position of opisthotonos. This position resembled that of persons afflicted with tetany. The head was carried backward, extended, and the jaws tightly closed, due to contraction of the muscles of mastication. The rigidity was sufficiently marked to make passive movements difficult or impossible. An attempt to move the limbs increased the rigidity. During the first four days after the operation the muscles occasionally went into spasms. No tremor was present except shortly before death. Chloroform and ether anesthesia dissipated the rigidity. The injection of tetanus toxin or strychnin has been shown by Claude and Lhermitte to increase it. This picture is in marked contrast to that produced by section of the cervical or dorsal portion of the spinal cord, for when this was done the muscles were in a state of complete flaccidity. The well-known fact that the voluntary muscles of the body are bilaterally innervated lead to the supposition that hemisection would not produce the state of rigidity identical to that produced by total section. This hypothesis was proved true by Sherrington. The animal showed a homolateral rigidity which was not as constant as in the completely sectioned animals. Nor was the position exactly the same. The tail curved but also deviated homolaterally. . The head was overextended but homolaterally directed. Lhermitte states that the homolateral forelimb was flexed. This is not Sherrington's or Wilson's statement. (Wilson, S. A. K.: *Brain* **43**:246.) The homolateral limbs were as in bilateral rigidity. The inconstancy of the rigidity suggested that the inhibitory activities of the intact half of the nervous system were in conflict with the released tonic centers of the operated half.

Lhermitte points out the importance of these experiments in formulating a conception of partial decerebrate rigidity. Having stated these experimental findings, Lhermitte describes the various interpretations which have been given them. He emphasizes the great importance of stimuli of a sensory character, either from special, general or visceral receptors. One method of cutting off the majority of these afferent stimuli is by section of the cord, and, as is well known, this, when attempted in hemidecerebrate rigidity destroys the rigidity and produces flaccidity. Supposedly section of the posterior roots destroys rigidity in the muscles segmentally related. To a certain extent this is true, but rigidity is not entirely absent. Furthermore, Brown has shown that stimulation of the midbrain in animals whose posterior roots had been cut would still produce rigidity in the muscles of the corresponding segments. Lhermitte observes that though the posterior nerves contain the majority of the afferent paths, some other pathway must exist. He mentions the work of Lehmann who showed that certain sensory fibers of visceral origin reach the spinal cord via anterior roots as a possible explanation.

The particular pathways within the spinal cord which carry sensations essential to the maintenance of rigidity and the experimental data showing that section of Gowers' tract in its entirety is not necessary to the maintenance of rigidity are then discussed. Cutting of the posterior columns and the track of Flechsig does not abolish rigidity. The work of Magnus and Kleijn showing that lateral movements of the head altered the position of the animal by stimuli passing through the vestibular apparatus and the cervical nerves, is mentioned.

Lhermitte leaves us without any clear notion of the exact afferent path concerned with rigidity as our present knowledge is not sufficient to define it. The center which controls tone is next considered. Lhermitte emphasizes again that this center lies somewhere between the upper portions of the midbrain and the caudal end of the medulla. He cites some of the evidence given to establish the part played by the cerebellum. However, this evidence, as he emphasizes, is by no means conclusive.

The nuclei of Deiters are next considered, and the work of Ewald which showed that the labyrinth exercised a tonic effect on voluntary muscles, is quoted. Sherrington and others have admitted that decerebrate rigidity and postural tonus are, in the major part, dependent on the integrity of the nuclei of Deiters. Thiele has shown that they are not the only factors. The red nucleus is next considered and the opinion expressed by Kinnier Wilson, as well as the evidence which this writer used, are offered to indicate that this nucleus plays a large part in the production of rigidity.

Lhermitte has omitted these observations of H. C. Bazett (*Brain* **43**:306 1920): "It is at any rate clear that decerebrate rigidity persists even after the rubrospinal tract is mostly degenerated, so that if the red nucleus is responsible for the rigidity it must be the lower part of this nucleus that is concerned; and it is established that the rigidity is not due to the excitation of nerve fibers divided in the operation, since in this case the rigidity could not be maintained after the degeneration of the fibers."

Summing up his information on the afferent and efferent paths concerned with tonus and posture found in decerebrate rigidity, Lhermitte states that the rigidity is due to the release of certain centers from the control of those parts of the nervous system lying above the cerebral peduncles. He calls our attention to the interesting observation of Sherrington that the rigidity

affects with the greatest intensity those muscles which are least affected by cortical stimulation and whose contractions under normal conditions are concerned with the maintenance of posture. He emphasizes the importance of the extrapyramidal motor system to which he gives the name tegmentospinal. One of the important functions of this system is the maintenance of posture. Lhermitte fails to define the type of posture to which he alludes. It is quite obvious that any position of the body can be defined as a posture. The particular postural activity to which he refers, by the general use of the term, should be defined as antigravitational posture. Surely the position of the arm in posthemiplegic contracture is one of posture and cannot be identified with the position of the arm in decerebrate rigidity.

The tegmentospinal extrapyramidal system is inhibited on two sides, on one hand by the cerebral cortex and on the other hand by certain parts of the striate body. The pathway of inhibition by the first of these is via the frontopontocerebellar tract and the pyramidal tract. Stimulation of the frontopontile tract in the internal capsule always inhibits decerebrate rigidity.

To sum up the evidence given, it would appear that a tonic center exists in the brain stem, which is influenced by the more cephalad portions of the brain. The exact pathways to and from this center or group of centers have, as yet, not been determined with decision.

Kinnier Wilson, stimulated by the physiologic experiments of Sherrington, attempted to demonstrate a syndrome of decerebrate rigidity in man similar to that established for animals. Wilson found that not only did a condition exist in pattern identical to that found in animals, but that it could be caused by various pathologic states. The pathologicophysiologic characteristic is interruption, either anatomically or functionally, of the connections which unite the forebrain (diencephalon, telencephalon) with the inframesocephalic portions of the cerebrospinal axis.

From a clinical point of view, cases of decerebrate rigidity are divisible into two large groups. The first comprises those in which the state of decerebrate rigidity appears and consciousness is completely abolished. In the second group consciousness is not abolished. As might be expected, the cases falling into the first group resemble more closely experimental results than those of the second group. In view of this, Lhermitte begins his review by a discussion of decerebrate rigidity and tonic attacks combined with coma. Wilson reports five personal observations in which the decerebrate attitude was combined with tonic attacks similar to those described by Hughlings Jackson under the name "tetanoid attacks" (*Brain* **29**:425, 1906). These attacks, attributed to lesions of the cerebellum, differed from those of cortical origin in that they were not clonic but tonic. Jackson emphasized this contrast and pointed out in addition that in the cerebellar attacks those muscles whose action was synergistic were involved. The attitude during an attack, which was identical to that of decerebrate rigidity, was due to contracture of the muscles of the neck, of the dorsolumbar region and of the lower extremities. Both in decerebrate rigidity and in cerebellar attacks the attitude of the patient is that of tetanic opisthotonus. The head is pulled back, the dorsolumbar region curved forward, the lower extremities extended, the arms half flexed. The patient cannot talk or swallow, the latter being due to trismus which maintains the jaws tightly closed. That attacks of this kind are related to cerebellar lesions has been demonstrated by many anatomicoclinical observations, among which may be mentioned those of Jackson, Stewart and Holmes, MacEwen, Dana,

Russel, MacRobert and Laurent Feinier. Lhermitte then proceeds to give in some detail several case reports of Wilson.

In the second group of decerebrate rigidity without loss of consciousness, Lhermitte emphasizes the various postural fragments of the state of decerebrate rigidity which Wilson has illustrated in his article. Lhermitte notes that the posture of spastic hemiplegia represents a fragment of decerebrate rigidity. It is interesting to note here that in typical spastic hemiplegia the elbow is flexed, not extended, so that though one might speak of the position in posthemiplegic contracture as one due to a degree of decerebration, it is quite certain that one would not be justified in identifying that position described by Kinnier Wilson as decerebrate rigidity with the position of posthemiplegic contracture as Lhermitte has tried to do, nor would one be justified in identifying the position found in animals by Sherrington with the position of posthemiplegic contracture. At this point it seems worth emphasizing that the words decerebrate rigidity may come to be used rather loosely. It would seem much better to speak of the position of decerebrate rigidity described by Kinnier Wilson as the position of antigravitational posture, for, as was emphasized in the early portion of Lhermitte's review, the position in decerebrate rigidity is essentially that produced by the response to the need of counteracting the effects of gravity.

Lhermitte proceeds to give several case reports from Wilson's paper which illustrate fragments of the posture of decerebrate rigidity. The postural defects in unilateral cerebellar disease are introduced into the conception of decerebrate rigidity. The postural deficiencies of chorea and athetosis are included. The postural defects of dystonia lenticularis are also included. Lhermitte refers to the work of Pal, who showed the influence of changes in arterial tension on the occurrence of various types of fits. Sudden increase of tension produced fits like the tonic attacks of decerebrate rigidity. These could be reproduced by the injection of epinephrin.

Lhermitte attempts an analysis of the pathogenesis of rigidity. He emphasizes the fact that in the relatively few cases which have come to necropsy the ventricles were distended, the intraventricular pressure increased. Lhermitte explains the appearance of rigidity by a physiologic block analogous to the anatomic section of Sherrington, caused by pressure on the upper portions of the midbrain by increased intraventricular pressure.

To sum up: One is impressed with one thing throughout. Hypertonus and posture are brought too closely together. They must concern different parts of the nervous system however close to each other these parts may be anatomically. There is little attempt to emphasize the fact that hypertonus flows into different postural designs, as for example, those of posthemiplegic contracture, decerebrate rigidity and the "flexion-reflex" posture of spinal disease.

The relation of the hypertonus to the involuntary nervous system is not emphasized. It is quite obvious that the involuntary nervous system is represented above the midbrain, that its primary neuron is cut by the lesion which causes the picture of decerebrate rigidity. Is the hypertonus a phenomenon of release due to this injury?

As has been noted in this review, the word "posture" or "attitude" is used too generally. Sherrington emphasized in several places the fact that in decerebrate rigidity the antigravity muscles are affected. Hence this posture should be designated as antigravitational posture.

KRAUS, New York.

SOME PECULIARITIES IN THE DEVELOPMENT AND IN THE MYELINIZATION OF THE SPINAL CORD. E. D'Abundo, Riv. ital. di neuropatol. psychiat. ed elettroter. **14**:65-93 (March) 1921.

The author has studied the development and the myelinization of the different sections of the spinal cord in human fetuses at various periods of growth (as old as six and seven months), in infants 5, 8, 44, 75 days, 3, 11, 14, 24, 36 months old, and in embryos of animals (*Mustelus levis, Torpedo occellata,* chicks and rabbits). He followed the development of the ependymal and the nuclear zones (gray matter), and of the marginal substance (white matter) of the spinal cord; the formation of myelin in the nervous fibers, constituting the different bundles and tracts, and the anterior and posterior roots; the myelinization of the anterior and posterior horn cells. Special attention was paid to the study of the cervical and lumbar enlargements. Two acephalic fetuses were also studied.

Fifty-two illustrations are included in the text. The article may be summarized thus: The differentiation of the gray spinal substance is more rapid in the anterior horn, and it manifests itself with a diminution of the condensation of the embryonal cellular elements; this condensation becomes more intense toward the posterior horn where it reaches its greatest density in the more peripheral zones.

In human fetuses a coordinate relation exists between the evolution of the ependymal zone and that of the nuclear zone. With the differentiation of the latter coincides a thinning of the corresponding ependymal zone which follows the same phases of differentiation of the nuclear zone, namely, it is maximal anteriorly and minimal posteriorly. This observation tends to confirm the fact that the anterior horn precedes the posterior horn in the histologic evolution. The most probable explanation of the phenomenon is to be found in the later dorsal closure of the medullary tube; the embryologic cause seems to account for the later differentiation of the posterior spinal portion in the first period of fetal life.

To the precocity and rapidity of development of the cervical enlargement (a fact which the author partially attributes to the precocity of the voluntary movements of the upper extremities) does not correspond a precocious myelinization of the intercellular fibers of the gray substance in the cervical enlargement, if compared with the lumbar enlargement; on the contrary, in the lumbar enlargement a more marked condensation of the medullated intercellular fibers, some of which are unusually large, is early visible. At the seventh month of prenatal life the myelination of the lumbar cord is by no means behind that of the cervical enlargement. This fact may be related to the medullary automatism of the deambulation having its center in the lumbar enlargement.

The myelination of the gray substance is decidedly developed at the sixth month of fetal life; however, the intercellular fibers are more markedly and more rapidly myelinated in the anterior portion. This condition is not due alone to the slower differentiation of the posterior horn but to the fact that the territory of the substantia gelatinosa of Rolando, although the richest in finer neurons, is poorer in medullated fibers, and its neurons possess delicate axis cylinders which are almost lacking in collaterals during their vertical transit through the spinal columns; besides, it is after birth that the fibers of the zona radicularis postero-lateralis of Flechsig, which go to the stratum spongiosum substantiae Rolandi dorsalis, are myelinized.

The anterior spinal commissure myelinizes early in fetal life and reaches its almost complete development during the first months of postnatal life. Through this commissure pass only a very small portion of the fibers constituting the column of Türck; the remainder of the fibers most probably run in a direct tract. The posterior commissure also undergoes an early myelination; however, this is slower in reaching its maximal development in postnatal life.

Already at birth there exists a maturity of the myelinization of the spinal cord sufficient to the immediate requirements of the life of nutrition and of the life of relation. This maturity takes place independently from the cerebrum, as demonstrated by the study of the acephalic fetuses.

The persistence of some fetal characteristics of the human lumbar cord even in the adult might explain the great predisposition of this section of the cord for the morbid localization of some neuropathies (acute poliomyelitis, myelitis, etc.). This fact tends to specify what may essentially signify the constitutional predisposition to diseases of determined portions of the spinal cord, in the presence of exogenous and endogenous morbid causes, especially when in the normal course of the embryonal development the posterior part of the medullary tube is subject to alterations and arrests of development.

NACCARATI, New York.

THE WASSERMANN REACTION IN CASES OF TUMORS OF THE CENTRAL NERVOUS SYSTEM. F. LOTMAR, Schweiz. med. Wchnschr. **51**:1013 (Nov. 3) 1921.

In 1910, Oppenheim and others reported cases of brain tumors with positive blood Wassermann reactions in which subsequent investigations and postmortem findings revealed no evidence of a syphilitic process. Since then several cases have been reported with similar findings. Nonne believes that only a positive Wassermann reaction of the spinal fluid is indicative of a syphilitic process in the central nervous system and that a positive blood Wassermann reaction alone has no significance. Other workers, however, disagree with Nonne's views as cases of meningitis, brain tumor and spinal cord compressions are on record in which a positive spinal fluid Wassermann reaction on later investigation proved to be nonspecific.

Lotmar reports a case of cerebellopontile angle tumor which at postmortem showed a xanthofibrosarcoma with no evidence of central nervous system syphilis. A spinal puncture in June, 1920, showed a strong positive Wassermann reaction in several dilutions with a positive Nonne reaction and six cells. Specific treatment was of no avail. A second spinal fluid examination in August revealed a negative Wassermann and a positive Nonne reaction. The postmortem findings revealed a tumor.

The author takes up the various possibilities which might account for the specific Wassermann reaction. He is inclined to look on the finding as a reaction frequently seen in certain diseases in which there is a central nervous system involvement, as in scarlet fever, pellagra and poliomyelitis. Positive Wassermann reactions of both the blood and spinal fluid have been found in other diseases, such as epidemic encephalitis, leprosy and tuberculosis. In the author's case the possibility of a coincident syphilis seemed to have been ruled out. Cases of tuberculous meningitis with a negative blood Wassermann reaction but a positive reaction in the spinal fluid have also been reported, and at postmortem examination syphilis could not be demonstrated. Of late

positive Wassermann reactions have also been reported in cases of epidemic encephalitis.

Regarding tumors of the central nervous system, several authors have reported cases with a positive Wassermann reaction in the spinal fluid. Müller reported such a finding in a case of cerebral glioma. A positive reaction has also occurred in extramedullary tumors of the cord, in compression myelitis due to tuberculosis and in neurofibromatosis. Since 1915, Nonne has seen two cases of tumor cerebri with positive blood and spinal fluid Wassermann reactions in which histologic examination showed no evidence of syphilis. Oppenheim reports a similar finding. Nonne says that this unusual reaction has not yet been explained. Stern reported a case somewhat similar to that of the author's in which the specific reaction was attributed to a tertiary malaria which the patient had had shortly prior to the onset of the tumor symptoms; this the author believes was an incorrect assumption.

The author believes that it may be possible for a positive Wassermann reaction in the blood to follow a central nervous system neoplasm. A positive blood Wassermann reaction is frequently seen in sarcomas and carcinomas occurring outside of the nervous system; the cases of Lotmar and Sterns might be considered in this group as they were both sarcomas.

In offering a possible explanation for this positive spinal fluid finding the author believes it possible that the tumor may cause lipoid changes which produce the specific reaction. Similar reactions have been obtained by Wassermann who obtained positive reactions in the spinal fluid by the injection of lipoids. Similar experiments have been performed by others. In his conclusion the author summarizes the findings in his case of xanthofibrosarcoma; he believes that in his case the nonspecific reaction was due to the tumor itself, probably to the formation of lipoids.

MOERSCH, Rochester, Minn.

TWO CASES OF CEREBROSPINAL CYSTICERCUS. L. REDALIÉ, Rev. neurol. **28**:241 (March) 1921.

Redalié directs attention to the difficulty presented by this condition from the standpoint of both clinical and histopathologic diagnosis. His protocols may be summarized thus:

The first case was that of a woman, aged 54, with a history of headaches and pain along the spine, dating back ten months. There was also equilibratory disturbance unattended, however, by loss of consciousness or vertigo. This condition persisted essentially unchanged until several weeks before death, when there were noted urinary retention, constipation with incontinence, marked general motor paresis, associated with fixation and dilatation of the left pupil, ptosis of the left eyelid and diplopia. In the sensorial field, there was determined definite diminution in general sensitivity almost to the degree of anesthesia. The deep reflexes were definitely exaggerated, with marked ankle clonus, and the Babinski and Kernig signs were strongly positive. Mentally the patient showed definite deterioration in all fields, particularly in the mnemonic. The spinal fluid showed a positive Wassermann reaction with marked lymphocytosis and albuminosis. Postmortem examination revealed a racemous cysticercus, involving the meninges on the ventral aspect of the brain, essentially in the intrapeduncular space, extending forward to the tips of the temporal lobes and posteriorly almost to the pons, with marked evidence of chronic meningitic involvement throughout this region, internal hydrocephalus and indication of obliterating endarteritis, implicating practically the entire

basal vasculature. The cervical cord showed another cysticercus, of the racemous type, involving the meninges ventrally and associated with marked chronic hypertrophic pachymeningitis. Degenerative changes were found in the spinal nerves of this region with atrophy of the anterior horns and softening in the posterior columns.

The second case was that of a man, aged 66, who had suffered epileptiform attacks for fifteen or sixteen years and who, for a year preceding his death, complained of difficulty in walking. There was later noted definite feebleness in the lower extremities and severe headaches. When seen by the author, some months prior to death, the patient showed marked mental deterioration, particularly in the mnemonic field. The pupillary reactions were sluggish, and there were also noted slight right hemiparesis, marked tremor of the extended fingers and tongue, with rigidity of the lower extremities and inability to walk. The blood Wassermann reaction was negative, and the spinal fluid Wassermann reaction was at first positive, but following a course of arsphenamin became negative, although there was persistent indication of pleocytosis. Postmortem examination showed very well marked cerebrospinal cysticercosis with a parasitic cyst of the floating type in the fourth ventricle. The base of the brain showed marked chronic meningitis with obliterating endarteritis of the basilar and sylvian vessels. The entire brain was somewhat atrophied with indication of internal hydrocephalus and granular ependymitis.

In commenting on these cases, the author remarks on the occurrence of the cardinal features usually described with cerebrospinal cysticercus—headaches, pupillary disturbance and paretic changes with epileptiform attacks and general psychic deterioration. The long duration in the second case possesses a certain interest as well as the fact that both of these cases seem to have been associated with syphilis, a feature rendering especially difficult the matter of exact diagnosis on a histopathologic basis. The author includes an excellent discussion of the literature, particularly from the semiologic standpoint.

RAPHAEL, Ann Arbor, Mich.

## FRACTURES OF THE SKULL: DIAGNOSTIC AND PROGNOSTIC FEATURES. J. W. STEWART, J. A. M. A. **77**:2030 (Dec. 24) 1921.

The author reviewed the records at the St. Louis City Hospital over a period of five years and found 6,135 cases of cranial injury. Of these 617, about 10 per cent., showed definite signs and symptoms of skull fracture. The average age was 36 years, and the sex ratio was 65 males to 35 females. Of the 617 skull fractures, 209 were basal; 408 were fractures of the vault, 198 depressed and 210 linear.

Roentgen-ray examination was positive in 73.1 per cent. and negative in 26.8 per cent. Three hundred and three patients, 49.1 per cent., were unconscious on admission to the hospital; 193, 33.2 per cent., were conscious, and 121, 19.5 per cent., semiconscious.

The author reviews the various immediate symptoms, such as vomiting, lowered pulse rate, and bloody or clear spinal fluid. Various neurologic examinations were conducted. The average pulse rate was 92 in patients who did not vomit and 83 in patients who vomited; this emphasized the point that the pulse rate was higher than is usually expected to exist in skull fracture cases. In 165 of the 617 patients a spinal puncture was performed and the cerebrospinal fluid found to be bloody in 90.5 per cent. Six of the fifteen patients with a clear spinal fluid proved to have linear fractures.

In a total of 209 cases of basal fracture, the pupils were equal and reaction normal in ninety-two cases, unequal and reaction normal in ninety-four cases, and equal, dilated and fixed in twenty-three. The various neurologic findings depended on the extent and degree of the injury.

In summarizing the final results of skull fractures, the author submits the accompanying table, but calls attention to the fact that operation was not performed in some of the more severe cases:

RESULTS IN SIX HUNDRED AND SEVENTEEN CASES

| Cases | Number of Cases | Died | | Recovered | |
|---|---|---|---|---|---|
| | | Number | Per Cent. | Number | Per Cent. |
| Nonoperative | 443 | 232 | 52.37 | 211 | 47.63 |
| Operative | 174 | 90 | 51.7 | 84 | 48.3 |
| Total | 617 | 322 | 52.19 | 295 | 47.81 |

ADSON, Rochester, Minn.

## ANISOCORIA DEPENDENT ON SYMPATHETIC REENFORCEMENT.

C. LAFON, Rev. neurol. **28**:274 (March) 1921.

The author calls attention to the fact that anisocoria per se need by no means be considered as preeminently syphilitic in basis or even necessarily of encephalic locus. He refers at length to the work of Roque and Sergent, indicating the importance of intra-abdominal and intrathoracic pathologic changes in the production of such changes, particularly the homonomous mydriases. The mechanism of causation in such cases, the author feels to be essentially excitation of a reenforcing or overflow character effective on the ipsolateral sympathetic pupillomotor fibers, produced in the passage cortically, through the medulla, of centripetal stimuli originally impinging on the sympathetic elements in the cord, from the intra-abdominal or intrathoracic points of specific lesion.

This disturbance appears to be essentially of a dissociating type, that is, it is characterized by mydriasis only and not by the complete sympathetic syndrome mydriasis, widened palpebral fissures, exophthalmos and hemifacial vasomotor constriction, thus indicative of effect on the pupillomotor fibers alone before they have become definitely organized in tract form with the other fibers of the series. This reenforcement stimulus augments the normal tonus of the pupillary mechanism but naturally on the side of dilatation and as the pupillary elements of the third nerve are not affected, the pupillary inequality produced is most manifest in faint light with no implication of the accommodation or light reflexes. This reaction, which may also occur in connection with dental or intranasal pathology and disorders of the external auditory meatus, Lafon terms the Roque sign. By the same token, in connection with irritant foci of an essentially intracranial nature, reenforcing effects may make themselves manifest on the parasympathetic elements of the pupillary complex with resultant homonomous myosis, also most prominent in dim light and unattended by change in the responses to light and accommodation.

In contrast to anisocoria due to actual intracranial involvement of the pupillary centers as such, where the light reflex is still present, this mydriasis and myosis, due to sympathetic or parasympathetic reenforcement, are most marked, as indicated, under conditions of feeble illumination and tend to

disappear under strong light, whereas the former is most noticeable under strong illumination and tends to become progressively less manifest with diminution in illumination intensity.

RAPHAEL, Ann Arbor, Mich.

PSYCHIATRY AND NEUROLOGY IN THE REVISED MEDICAL CURRICULUM. K. BONHOEFFER, Monatschr. f. Psychiat u. Neurol. **48**: 327 (Dec.) 1920.

". . . But it is not sufficient that the student learn in a general way what are the criteria of organic and functional nervous diseases; and what he is to do when he meets with a mental case. Many of the older practitioners feel that the duty of a psychiatric clinic is exhausted when it makes a diagnosis of a mental disease and determines the question of commitment. But the psychiatric and nervous clinic has a wider, and perhaps more important, duty. It must make the student appreciate the significance of the psychic not only in psychopathology, but in the whole field of medical practice. A little of this he may get in his general clinics. But the essential tendency of the general clinic is toward the material—the objectively demonstrable; and we realize from a survey of average medical practice that psychic and psychically induced symptoms are not fully appreciated. Were the psychic better understood, we would not have the eternal search for local findings to explain every symptom. The physician forgets that there are innumerable anatomical anomalies which are a matter of utter indifference to the psychically normal individual; anomalies which never produce a symptom and never cause him to consult a physician. How many times do uterine displacement, floating kidneys, gallstones, enteroptoses, septum deflections, swollen turbinates and enlarged tonsils gain significance simply because the physician in his search for the objective unnecessarily directs the attention of his psychoneurotic patient to them. How many unnecessary operations are performed simply because of misinterpretation of subjective complaints, to say nothing of how much compensation is unnecessarily paid because the physician assumes an organic trouble when as a matter of fact the subjective complaints are psychic in origin—dependent on a desire for compensation. And it is not only a failure to recognize the hysterics—this mistake is not as common as the failure to recognize depressive attacks, the manic depressive constitution and other psychopathies, masquerading under the guise of local diseases. Much of the success of the quacks is due to the fact that physicians undervalue or wholly fail to recognize the psychic element in disease causation. There is no doubt but that this phase of psychopathology is an important part of the general training of the physician."

SELLING, Portland, Ore.

A TENDON TRANSPLANT FOR INTRINSIC HAND MUSCLE PARALYSIS. K. WINFIELD NEY, Surg., Gynec. & Obst. **33**:342, 1921.

The author says that the results observed following suture of the peripheral nerves have surpassed all expectations. The apparently slow rate of regeneration through the distal segment of a sutured nerve is, however, often discouraging to the patient. It may be necessary to wait many months before an objective sign of a successful suture appears, that is, the return of voluntary power in the formerly paralyzed muscles.

The return of voluntary power is first observed in the larger muscles, and, although very slight at first, it gradually increases. The smaller and more distally located muscles, such as the intrinsic muscles of the hand and foot, are the last to manifest return of voluntary motor power. This is due to their distal location and the great amount of time required for the regenerating motor neuraxons to reach the end plates in the muscle fibers. Another factor of great importance is the muscular volume of these intrinsic muscles; this is so small that during the long period of paralysis, before the regenerating neuraxons can reach them, they have undergone marked atrophy and retain little of their former muscular tissue.

In combined median and ulnar nerve paralysis regeneration of the extrinsic muscles is more or less complete in from twelve to eighteen months following successful nerve suture. In a series of forty-two cases of combined median and ulnar paralysis with successful restoration of most of the extrinsic muscles only three showed, on last observation, any evidence of returning voluntary motor function in the intrinsic muscles of the hand supplied by these nerves.

The author had extensive experience in peripheral nerve surgery during the war in General Hospitals No. 3 and No. 41 of the United States Army and is convinced that some of the intrinsic muscles of the hand fail to function, even though there is partial regeneration in the larger muscles. One of the most serious of these failures is lack of regeneration in the thumb. In order that the thumb can be extended as well as flexed and the hand made more useful, he has devised a plastic operation on its tendons.

In résumé, the author calls attention to the important fact that the neurologic surgeon interested in nerve anastomosis should not forget the possibilities offered by tendon transplants when regeneration fails.

ADSON, Rochester, Minn.

## CLINICAL AND ANATOMIC CONTRIBUTION TO THE KNOWLEDGE OF THE LENTICULAR NUCLEUS (A CASE OF WILSON'S DISEASE). G. BORSARI and G. BIANCHI, Quad. di Psichiat. **8**:9-10 (Sept.-Oct.) 1921.

A girl, 13 years of age, intra vitam showed hypertonus, contractures, especially in the muscles of the extremities, and disturbances of deglutition and speech disorders, which began as dysarthria and which reached the degree of anarthria. Although the disease was in an advanced stage, there were no tremors, no convulsions and no psychic alterations. Necropsy revealed bilateral degeneration of the lenticular nucleus without a lesion in the internal capsule, cirrhosis of the liver with large nodes and a large splenic tumor. There was microgyria in the frontal lobes, especially on the left. No syphilitic changes could be demonstrated.

The authors conclude that this case, in which there were deep lesions without involvement of the internal capsule, clearly confirms the relationship of the lenticular nucleus to the motor functions, and demonstrates the possibility that deep destructive lesions of the lenticular nucleus may exist with complete integrity of the sensory functions. They see in this case a proof against the conception of Déjerine who believed in the involvement of the internal capsule in Wilson's disease.

After discussing the symptomatology of the lenticular nucleus the authors conclude that a correlation must exist between the lesion of this nucleus and pseudosclerosis of Westphal-Strumpell, Huntington's chorea, dystonia mus-

culorum deformans of Oppenheim, Parkinson's disease, spasmodic pseudobulbar paralysis with contractures and choreic-athetosic movements of Oppenheim and Vogt, progressive athetosis and apoplectic amyotonia of Bechterew.

NACCARATI, New York.

THE NATURE OF CHOREIFORM MOVEMENTS—CAN THEY BE INTERPRETED AS REFLEXES? ANDRÉ-THOMAS, Presse méd. **30**: 25 (Jan. 11) 1922.

Two cases in which the patient exhibited choreiform movements are discussed, with numerous illustrations. One showed pyramidal and cerebellar signs, and synkinesis was marked. Synkineses appeared not only with the upper and lower extremities, but also with movements of the head, tongue and eyes. The movements which were produced on the left side when the right extremities or the head were moved gave the impression of reflex rather than of associated movements. This impression was even more definite when one used other means of stimulation, such as pricking or tickling. For any given point of stimulation, provided the stimulus was sufficiently strong and prolonged, the reaction appeared promptly and in a constant direction. The response was livelier in proportion to the degree of stimulus. Pressure on a given area excited a response, but if the pressure was maintained with the same intensity, the response ceased. The phenomena of decerebrate rigidity are compared.

Movements in the second case were those of typical Sydenham's chorea, but they did not appear spontaneously, and synkineses were exceptional. The movements were induced, not by peripheral stimulation as in the first case, but exclusively by conversation and by a certain degree of psychic activity. In both cases the choreiform movements were excited in an apparently reflex manner. Such "reflexes" are doubtless different from those ordinarily included under that name, and yet the reflexes already known are not all necessarily referable to the same mechanism. The list of reflexes might be enlarged and revised.

HUDDLESON, New York.

TECHNIC OF NERVE SURGERY. K. WINFIELD NEY, Ann. Surg. **73**:37, 1921.

The author submits a very straightforward article emphasizing the important steps in nerve repair based on an experience of 300 peripheral nerve operations and personal supervision of 1,500 such cases.

Ney advises local anesthesia, with 1 per cent. procain solution containing 15 drops of epinephrin chlorid (1:1,000) to each 30 c.c. of solution. The "non-touch," or purely instrumental, nerve suture is advocated with great stress on the accurate approximation of severed ends and the avoidance of torsion. Moderate primary stretching of flexion relaxation, transposition, two stage operations when necessary, and only occasional use of autogenous cable grafts may be used in overcoming nerve gaps.

The author has used several homografts, refrigerator stock, with unsatisfactory results; in a few patients the autograft has proved partially successful. He lays stress on the preparation of the nerve bed, freeing it from scar tissue, and transferring the nerve into planes of normal tissue. He discourages the use of fascia lata, veins, Cargyle membrane, tubes, and so forth, and emphasizes the importance of avoiding injury to the nerve itself. Suturing is accomplished by fine silk epineural sutures, approximately eight in number. Neurolysis should be employed more frequently and even in cases of ischemic paralysis, dividing the epineurium and perineurium, and isolating the funiculi.

ADSON, Rochester, Minn.

ON THE GROWTH OF THE LARGEST NERVE CELLS IN THE SUPERIOR CERVICAL SYMPATHETIC GANGLION OF THE ALBINO RAT FROM BIRTH TO MATURITY. CHI PING, J. Comp. Neurol. **33**:281-311 (Aug. 15) 1921.

ON THE GROWTH OF THE LARGEST NERVE CELLS IN THE SUPERIOR CERVICAL SYMPATHETIC GANGLION OF THE NORWAY RAT. CHI PING, ibid., pp. 313-338.

These two papers contain the report of a study of the changes in size and morphologic characters of the largest cells of the superior cervical ganglion in the post natal development of three groups of rats: standard albinos, inbred albinos, and wild Norway. In standard albinos between birth and maturity the diameter of these cells increases about 55 per cent., and the increase in the nuclei is less than half this amount. The nucleus-plasma ratio increases from 1:4 at birth to 1:12 at maturity. In adult inbred albinos the nuclei are the same size as in the standard strain, but the diameter of the cells is less. The nucleus-plasma ratios in the inbred albinos are about half as great as in the corresponding cells of standard albinos. In the wild Norway rat the nucleus-plasma ratio increases from 1:5 at birth to 1:12 at maturity. The diameters of nuclei are the same as in standard albinos, but those of the cell bodies are slightly less.

C. J. HERRICK, Chicago.

VISUAL DISORDERS AFTER LOSS OF BLOOD. A. TERSON, Presse méd. **29**:974 (Dec. 7) 1921.

Single or repeated losses of blood occasionally bring on various visual disorders, which may be accompanied by definite blindness with optic atrophy, this last complication being relatively rare. Ordinarily the visual trouble appears between three and eight days after the loss of blood—never before the third day nor after the third week. It may take the form of (1) hemeralopia, quickly recovering; (2) homonymous hemianopsia of cortical origin, without eyeground changes and with fixed scotomas; or (3) diminution in acuity of vision, bilateral or unilateral, progressing rapidly toward partial or complete blindness, and ordinarily incurable.

These disorders occur most frequently after 40, and in women. Hemorrhage from any cause may be the cause. The optic lesion is most often peripheral; other cranial nerve or polyneuritic disturbances may occur at the same time. The mechanism is obscure; the author does not believe that ischemia alone or arterial hypotension is responsible, but he is inclined to believe that anaphylactic phenomena are involved. Possibly products of degeneration are absorbed from the wound, causing a special neurotropic toxemia. Necropsies have shown an ascending atrophy of the optic nerve, beginning peripherally with retinal lesions and without signs of infection, inflammation, embolism or thrombosis. (It is of interest to compare with this article a recent American Report on "Optic Neuritis in Serum Sickness" by V. R. Mason, *J. A. M. A.* **78**:88 [Jan. 14] 1922.)

Treatment is to be directed against ischemia and toward moderate congestion. Stimulants, transfusion and certain local operative measures are also suggested.

HUDDLESON, New York.

# Society Transactions

## BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

*Regular Monthly Meeting, Dec. 15, 1921*

JAMES B. AYER, M.D., *President, in the Chair*

### INFLUENCE OF VISION ON NYSTAGMUS. DR. C. L. WOOLSEY.

Isaac Jones has said, "The intimate relation between the ear and the eye can be best appreciated when we realize that the ocular mechanism depends upon stimuli from the ear for precision of movement." The intimacy of this relation may be greater than anticipated, if we note the inhibitory influence of vision over the outward manifestations of vestibular function.

There has been a great deal of discussion since the time of Flourens (1828) in regard to the cause of the "compensatory movements" or "with nystagmus" during rotation. When a normal pigeon is rotated, head free, certain movements of the head are noted, that is, the head seems to move slowly away from the direction of rotation, then quickly in the direction of rotation. These movements are called the "with nystagmus." Gruenberg (1907) thinks the compensatory movements may be due to the constantly changing view, but further states, "They may also be quite independent of visual impressions. One is therefore driven back to a reexamination of the semicircular canal theory, or to search for some other percursory movements or acceleration." Together with Prof. Wills he concludes that the "compensatory movements" are due to the spin which objects are subject to, when rotated. Isaac Jones (1918) states, "During the turning there is a vestibular pull of the eyes to the left, that is to say, a nystagmus toward the right"—when rotating to the right. Rizto, London (1920), concurs in this belief, briefly summed up, "The semicircular canals produce the compensatory eye movements when the head is in motion." In performing a number of experiments on the vestibular apparatus of the pigeon, it was evident that the "with nystagmus" of head or eyes during rotation depended in frequency on the rate of rotation, ranging from one to twelve movements of the head through 360 degrees. It was noted that the eyes did not enter into the movements per se, if the head was free to move, but if the head was stationary the eyes moved. It seemed probable that vision was partly responsible for these movements on account of the range from one to twelve. Vestibular stimuli could hardly produce such a variation, consequently numerous methods were employed to overcome vision without destroying sight, but all proved unsatisfactory. Following a suggestion of Dr. Stanley Cobb, experimental amblyopia was attempted. This was best secured by injection of a saturated solution of ammonium sulphate into the retina, which produced amblyopia without destruction of the iris, allowing subsequent interpretation of nystagmus with ease. Jones states that it requires approximately ten rotations of a human being to cause the "after nystagmus." Ten rotations of the normal pigeon in ten seconds produced an "after nystagmus" lasting for 3.2 to 4.6 seconds. When a pigeon with experimental amblyopia was rotated head free one revolution in ten to twenty seconds there was no compensatory movement

or "with nystagmus" of either eyes or head, which seems to refute the idea that the "with nystagmus" was due to "vestibular stimuli." The contention may be raised that the rate of rotation was too slow to produce any movement of the endolymph, but this is erroneous since the same pigeon with amblyopia, when rotated one revolution in 20 seconds, developed no "with nystagmus," but an "after nystagmus" lasting for from 5 to 6.1 seconds. When rotated one-half turn in 10 seconds there was no "with nystagmus" but an "after nystagmus" lasting for 3.1 seconds. When rotated one-quarter turn no "with nystagmus" developed, but an "after nystagmus" of 2 seconds' duration. When rotated ten times in 10 seconds there was a "with nystagmus" and an "after nystagmus" lasting for 12 seconds. The "with nystagmus" was due to the head being pivoted and not able to keep up with the body, hence a twisting of the head away from the direction of rotation. This "twist" disrupts the muscle balance, which is the stimuli that causes the correction and thereby produces the "with nystagmus."

In conclusion: In the normal pigeon it requires at least five revolutions to produce any appreciable "after nystagmus," which is always accompanied by a "with nystagmus." With experimental amblyopia only one quarter of a turn in five seconds is required to produce an "after nystagmus" of two seconds' duration, which is not preceded by a "with nystagmus," which when compared with the normal pigeon shows the profound influence of vision on nystagmus. (A Preliminary Report of Experiments Being Done on Vestibular Apparatus of the Pigeon in the Neuropathological Department of the Harvard Medical School.)

## PROGRESSIVE MUSCULAR DYSTROPHY IN A MOTHER AND THREE CHILDREN. Dr. H. B. Eaton.

Looking through the literature on this type of disorder I find that we are in about the same position regarding it as we were in 1886. The family shown is a particularly good illustration of the disease. The mother says that she first noticed her difficulty when she was 15 or 16 years old by a weakness of the arm which she attributed to falling out of a swing. The two oldest children, 13 and 12, have noticed for four or five years that they were unable to do what their friends did. The second boy, for instance, could not play basketball. The little girl of 6 has no trace of the disease so far as I am able to find. In the woman the reflexes are absent. In the older boy there are no tendon reflexes, but in the other boy they are diminished but present. The boys react to faradism but the mother does not.

### DISCUSSION

Dr. F. J. Farnell: I have had under observation for the last seven years a Jewish family of three boys and two girls, with dystrophy. The oldest boy, 16 years old, has fully developed pseudomuscular hypertrophy with an inability to move about. The second is a boy of 13 who has a full fledged case and has to be carried to school. In the third child, a boy of 11, the disorder is fully developed. The fourth and fifth children, girls of 8 and 6 years, are quite well. There is no evidence of this disorder in either side of the family. A rather interesting feature is the effect of sugar on these cases. By feeding them a great deal of sugar and raising their tolerance they become more active, and the two boys who are able to get about seem to last longer at their play. The sugar content in the blood on a starvation diet is usually 90 mg. per 100 c.c. of blood which is somewhat low. The tolerance stays up

on the sugar diet. Whether this has any significance in the interpretation of the disorder I really do not know. When the first boy came under my care about eight years ago I began to give him very large doses of pineal gland and for a while he seemed to improve and hold his own. The only additional experience I have had with endocrine glandular substance in relation to pseudomuscular hypertrophy was a marked case of pseudohypertrophy in which the patient for five years has been under large doses of pineal gland, and the disorder today is no further advanced than it was five years ago. In this case also the blood chemistry in relation to the sugar metabolism showed a similar picture. The method which has been used in feeding for sugar tolerance is to give an ounce of honey, preceding the induction by a blood sugar test, and then in one hour to make another examination for blood sugar; a third examination is made two hours after the honey is taken. In these cases the sugar content of the blood will remain up longer than normal. In a normal person the tolerance will rise within the first hour and it will drop to approximately normal by the end of the second hour, which, as I understand, indicates a normal sugar retention. Should the sugar content in the blood remain up at the end of the second hour it is called a high sugar tolerance.

DR. D. J. MACPHERSON: We have one boy of 12 with this condition which started when he was about 7 years old. He has an infantile sella. I gave him pituitary substance and could see no difference except the effect it had on his headache which he had on an average of once every ten days or two weeks. In about six months he reported that he had had no headache during that entire time. Aside from that, there was no particular change in his condition. I used the whole pituitary.

## THE USE OF SODIUM CHLORID IN CONCUSSION OF THE BRAIN.

Presentation of Cases. DR. HUGO MELLA.

Many patients who have received blows on the head develop headache of an extremely persistent type—often this headache does not commence until anywhere from several hours to a week or two after the injury. These headaches are not relieved by the ordinary remedies nor can they always be considered as the result of malingering to aid the patient in obtaining compensation, as they often occur in those cases in which this problem is not involved.

Venous congestion in the fundus of the eye or even choked disk may be found, but ordinarily nothing abnormal is elicited on physical examination; all that we find is a history of headache coming on after the cranial injury. It being a well-known fact that severe concussion of the brain may cause an edema of such a degree as to require decompression operations to save vision, if not life, I have thought for some time that those patients who have only headache might very well have an edema of the brain of a moderate degree and that if this fluid could be removed from the brain and the cerebral blood vessels be relieved of this pressure so as to reestablish a normal circulation, the headache would disappear.

In 1919, Weed of Baltimore reported in the *American Journal of Physiology*, that the injection of a 30 per cent. solution of sodium chlorid or a saturated solution of sodium bicarbonate into the circulatory system would reduce not only the cerebrospinal fluid pressure but also brain bulk. This reduction of cerebrospinal fluid pressure and brain bulk also results from the introduction of a hypertonic solution into the intestinal tract. It would not be practical to use the intravenous method in ambulatory cases, so, when the patients can

tolerate it, I have them drink the salt in solution, as I believe that if a hypertonic solution will reduce brain bulk experimentally in the lower animals it might relieve these cases of "mild" edema of the brain. Should the patient be nauseated by the salt solution, I have the salt put up in capsules of 0.5 gm. each. Weed has found that the approximate dose is 1 gm. to every 10 pounds (4.5 kg.) of body weight and has had enteric tablets of 1 gm. each made up which are now on the market, but I have obtained results with both the solution and the capsules as illustrated in the following cases:

CASE 1.—Massachusetts General Hospital; S. L., aged 20, a man, white, single, an order clerk, April 16, 1921, fell 3 feet (0.912 meter) from a freight elevator. He was not unconscious; he had a slight dizziness for one day, then a frontal headache came on which was not severe but constant. There was no ringing in the ears. The patient had a small clean wound on the back of the head; there was no swelling and no surrounding tenderness.

The pupils were equal and reacted to light and distance. There was no nystagmus; the fundi were essentially negative. The tongue protruded in midline. The knee and ankle reflexes were equal and active. The plantar reflexes were normal. Sodium chlorid was prescribed, ½ dram (2 gm.), in water three times daily.

April 18, 1921: The patient felt better for about three hours after taking salt. The headache was relieved but returned gradually. Sodium chlorid was administered, 1 dram (4 gm.), in water, every four hours. April 20, 1921: The patient had no headache except a little after riding on a street car on the way to the hospital. He was advised to return to work. Sodium chlorid was administered, 1 dram three times daily, for one week then twice daily for one week. May 4, 1921: The patient's condition had improved. He had no headache; he lived an outdoor life. May 18, 1921: He had no headache and no nerve lesion. Dec. 12, 1921: The patient was entirely well; the headache did not return.

CASE 2.—Massachusetts General Hospital; R. M., aged 14, a white schoolboy, Nov. 22, 1921, about two months before presentation, fell from a team and struck the back of his head and neck. He said that he was all "mixed up" and out of his head immediately after the accident but his condition rapidly cleared up. Two weeks later he "went out of his head" and has been irrational ever since. He is now mentally retarded. He responds slowly to questions and is very deliberate in speech and movements. He has no convulsions. He complains of headache. He is said to have been normal before the accident. There is no external evidence of injury to the skull or spine. A roentgenogram of the skull and spine was negative. There were slight venous congestions of the fundi; there was no choked disk. He had diplopia, but it was not constant. One-half dram sodium chlorid (in capsules) was administered four times during the day and night. Nov. 23, 1921: The patient was brighter and responded to questions very well. He said that he had a dull headache, but it ceased after taking salt. One-half dram sodium chlorid was administered three times daily. The dose was gradually reduced in one week to once daily. Nov. 29, 1921: The patient did not have headache. The fundi were negative. He received one-half dram of salt three times a day. Dec. 6, 1921: The patient was improving; he had no headache; he was still a little slow in responding to questions. Continued salt administration, one-half dram in the morning. Dec. 13, 1921: The patient had no headache. Salt administration was discontinued. Dec. 15, 1921: No salt was given. He complained of numbness in the head; he responded poorly to questions and appeared

quite disturbed. 8:30 p.m.: The patient was given salt by mouth; at 9:30 he had quieted down slightly but was still quite disturbed. Salt was discontinued too soon.

DISCUSSION

DR. F. J. FARNELL: Probably some of the members of this Society recall a case of oidiomycosis presented by me about three years ago. The patient showed lesions on his chest and spinal column. He was treated with potassium iodid. It required 400 grains (26 gm.) of potassium iodid a day to keep his disease in check. The man finally recovered and lived until about a year and a half ago, dying from pneumonia. His family physician said emphatically that the man did not have the oidiomycotic infection at the time of his death. The percentage of potassium iodid that the man was taking led me to feel that it might be possible to attack the problem in a different manner. The next case coming under my observation was at the State Hospital. I made a 25 per cent. solution of potassium iodid and gave him 200 c.c. intravenously. Within a few days the man improved and gradually recovered. He is perfectly well today and shows no evidence of his disease so far as known. At that time he had skin lesions as well as a cerebrospinal disorder. Last April a child was brought to me with this disease. I gave her a 10 per cent. solution and all lesions subsided immediately. The use of hypertonic sodium iodid solution intravenously as applied in fungus disease naturally led me to feel that it might be used for other purposes, and for two years past I have been giving hypertonic sodium iodid intravenously to three types of patients: first, to those with oidiomycosis, which cases are cleared up almost immediately; second, to those with the meningitic and meningovascularis forms of syphilis. These are treated with a 10 per cent. solution of sodium iodid intravenously followed by arsphenamin. Third, to those with hyperemic headache, not the headache due to a blow but that which occurs periodically and which is so severe as to keep the patient in bed for two or three days—the type that manifests complaints of an ocular type. A series of patients with hyperemic headaches have responded immediately to a 10 per cent. solution of sodium iodid. The usual procedure is to give intravenously 100 c.c. of a 10 per cent. solution of sodium iodid every five days (made up fresh).

DR. W. J. MIXTER: I am naturally very much interested in this subject from the surgical point of view. We tried the use of hypertonic salt solution intravenously in a small series of severe cranial injuries without much effect. They were all severe and some of them were complicated cases. My own feeling is that the main effect in the traumatic case as in any other type of case treated with hypertonic salt solution is on the cerebrospinal fluid, and that there is probably comparatively little effect on the brain. The work that Dr. Mella is doing should be followed out in a larger series of cases and in the more severe type of concussion, if possible, the type in which the patient is kept in the hospital. I feel that severe concussion is definitely a subject for hospitalization and cases can probably be followed there better than in any other way. We must remember that there is a definite rebound after the use of hypertonic salt solution, and we must be careful that our rebound is not enough to give us increased symptoms. Looking back fifteen or twenty years we find that one of the prime requisites in the proper treatment of concussion in this hospital was the most active purgation by salts. That method was dropped about the time I was house officer as being empirical and probably of no value; I doubt that it has been carried out at all during the last few years. I believe that such purging had the same effect as the salt solution.

DR. DONALD GREGG: Hypertonic salt solution in the form of Epsom salt has been used by most of us for years with some success, possibly only transient, in three kinds of cases—headache, acute alcoholism and epilepsy. Perhaps, instead of lessening "autointoxication" or some other unproved condition, we have been dehydrating the central nervous system a bit. Possibly also, the new treatment of epilepsy by starvation obtains results by a similar physiologic method.

## THE SPINAL FLUID IN MULTIPLE SCLEROSIS. DR. H. B. FOSTER.

Dr. Foster gave a preliminary report on his laboratory work with the cerebrospinal fluid in multiple sclerosis. He said that the thirty-eight cases had been selected with due caution. The fluids all presented a negative Wassermann test. The cell counts were from normal to a marked increase (50 per mm.). The total protein content, quantitatively determined by the Denis-Ayer method, was from normal to nearly three times normal. In a relatively small number of fluids a globulin ring with ammonium sulphate was present. The colloidal gold solution test gave a curve in the so-called (misnamed) paretic zone in half of all the fluids. However, if only those cases showing a progressive activity, clinically, were grouped together, the percentage giving this zone curve was considerably higher. The sugar, nonprotein nitrogen, urea, uric acid, creatinin, acetone bodies and chlorid content were well within the normal limit of range. Blood correlations were made performing the biochemical tests enumerated in the foregoing, and the results were all within normal limits, with one exception. The blood Wassermann reactions were also negative. The noteworthy feature of the laboratory findings in the cerebrospinal fluid from patients with multiple sclerosis, then, is the seeming approach to a normal fluid, the colloidal gold solution curve being a frequently occurring exception.

(The full report of this work was given before the Association for Research in Nervous and Mental Disease in New York, Dec. 28, 29, 1921. This report will appear in the ARCHIVES OF NEUROLOGY AND PSYCHIATRY.)

## BULLET WOUND OF THE BRAIN. DR. E. W. TAYLOR.

The following case is reported because of the unusual sequence of events in its course, especially the relation of trauma to what appeared to be epilepsy, the relief of epileptiform attacks by operation and the subsequent production of a hemiplegia with partial hemianesthesia and possibly symptoms relating to the thalamus.

The patient, a man of 32, stated that he was accidentally shot at the age of 5, the bullet lodging in the brain somewhat near the surface. No operation was performed, he made a good recovery, became a ship mechanic, was admitted to the Army, and worked in a ship yard. While at this work in November, 1916, he fell a distance of from 40 to 45 feet (12.16 to 13.68 meters) and became unconscious but was not paralyzed. Thereafter he had severe headache and in the latter part of the month in which he was injured an epileptiform attack with apparently definite loss of consciousness. These attacks increased greatly in frequency and finally led to operation which resulted in the removal of part of the bullet but unfortunately with a resultant hemorrhage which destroyed a considerable portion of the parietal region of the brain on the right. From this developed a severe left hemiplegia, naturally without aphasia. The epileptiform attacks ceased and he has had no recurrence or headache in spite of the destruction of brain tissue following opera-

tion. He later developed a slight hemianesthesia and sudden attacks of pain which pointed somewhat toward the thalamus. His condition has not materially improved in spite of assiduous treatment.

DISCUSSION

DR. W. J. MIXTER: This patient at operation showed a simple cyst and about it the fragments of the bone to which a considerable fragment of lead was firmly adherent. On loosening the indriven fragment of bone, which measured 3 or 4 cm., there was profuse bleeding from one of the arteries of the brain which had to be checked with a tie and packed. The result was paralysis which is now present. I think this shows clearly how extremely little damage to the brain will cause a rather severe type of palsy. I had no idea that he would have left-sided paralysis when he came out from under the influence of the ether. It was impossible at the time of operation to remove the other fragment of lead which is still in place. I think one of the interesting points in this case is the fact that the patient has had no epileptic attacks since operation. Whether they will recur or not is a problem.

DR. J. B. AYER: To what were the epileptic attacks due?

DR. W. J. MIXTER: The attacks were probably due to the cyst and the indriven pieces of bone.

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## NEW YORK NEUROLOGICAL SOCIETY

*The Three Hundred and Ninety-Third Regular Meeting, Jan. 3, 1922*

FOSTER KENNEDY, M.D., *President*

### CHEMISTRY OF PHOSPHORUS IN BRAIN ACTIVITY. Presented by DR. WILLIAM H. PORTER.

Phosphorus in combination with soda serves the physiologic economy in three distinct processes: (1) In connection with the digestive functions the trisodic phosphate is acted on by the hydrochloric acid and converted into (2) a disodic monohydrogen phosphate which is the true alkalinizer of the body fluids and tissues. A high state of alkalinity is essential to perfect oxidation and assimilation. (3) After the disodic monohydrogen phosphate has served its purpose in the body it is excreted through the kidneys, where it meets a molecule of uric acid and is transformed into the acid monosodic dihydrogen phosphate, the true acidifier of the urine.

Phosphorus is found also in combination with calcium, magnesium and potassium, the sodium and calcium combinations being most important. Phosphorus also reaches the body fluids and tissues in the form of lecithin, nucleoalbumin, nucleic acid, phytin, etc. Phosphorus enters plant life as a phosphate to be synthesized into these highly complex bodies.

My contention for years has been that oxidation reduction takes place only in the fixed cells, as found in the various body glands, and not in the body tissues and fluids; and that this process constitutes, in a large measure, the biologic activity of the body cells. In connection with these oxidation reduction processes and the exact place where they occur, it should be remembered that the ganglion cells of the nervous system are large masses of protoplasm

resembling in composition, but not in shape, the cellular structures of the glandular organs, and that, in all probability, they are the place at which the complex phosphorus-bearing bodies are oxidized and reduced.

The reasons for this interpretation are that these protoplasmic masses are abundant in the central nervous system; that these phosphorus-bearing compounds are found in larger amount at this point than in any other parts of the body, and that there seems to be a decided generation of impulses originating in the central nervous system which control and regulate the automatic balance of the human system—a condition which could not be maintained if the nervous energy was due solely to reflected heat energy brought to the central nervous system by the centripetal nerves and reflected out again by the centrifugal nerves. Active working of the central nervous system is always accompanied by increased elimination of alkaline phosphates, which fact tends to support the theory that these phosphorus-bearing bodies are oxidatively reduced in the cells of the central nervous system. Hence, increased elimination of the alkaline phosphates indicates simple augmented physiologic activity of the nervous system; and overelimination of the earthy phosphates in a highly acid urine indicates a malnutrition involving chiefly the nervous mechanism.

The answer to the question as to how these complex phosphorus-bearing bodies can be converted into energy and phosphates, and how they pass out of the system, is plain if the theory be accepted that the protoplasmic masses of the central nervous system have the power oxidatively to reduce this class of bodies. Assuming that the nerve cells possess this power, lecithin, for instance, is here reduced to phosphate of soda, urea, carbon dioxid and water.

It is recognized that bone deficiency is not due to lack of lime salts or bone-producing elements, but to disturbance of metabolism which prevents fixation of the calcium salts. In the reduction of the phosphorus-bearing molecule it is reasonable to suppose that, for an instant, the phosphorus atom is free and exerts this oxidative stimulating action on the protoplasmic masses, thus generating an inherent central nervous impulse, which not only augments the cell activity per se in which this change occurs, but is reflected to all parts of the economy by the nerve fibers springing from the cells.

So far as known to the author, the production of disodic monohydrogen phosphate from these complex phosphorus-bearing compounds is a newly revealed fact, and gives to the physiologic economy an inherent source of this absolutely essential body alkalinizer. How much is produced in this manner daily is not known.

## A CASE WITH THE CLINICAL PICTURE OF MIDDLE FOSSA TUMOR: NECROPSY FINDINGS. Dr. E. D. Friedman.

John C., 11 years old, an Italian, admitted Nov. 13, 1921, to Bellevue Hospital, died Dec. 11, 1921. The family history was negative. His delivery and development had been normal. His present illness began from five to six months ago with attacks of headache lasting about one day and occurring once a week. His condition remained unchanged for three and a half months. He then became bedridden, being unable to walk. Three weeks prior to his admission to the hospital he became drowsy and had nose bleed; the right eye became blood-shot. Weakness of the right side of the face developed. There was no fever at any time. Three weeks ago at the onset of one of his attacks he was unconscious for a short time. His headache became constant, but there were no bladder or rectal symptoms. He had complained of

pain in the right side of the face and of double vision. Physical examination revealed an emaciated, pale boy, with a dry skin, with no abnormal medical findings. He was irritable and cooperated poorly in the examination. The right pupil could not be examined, due to local conditions in the eye. The right fundus could not be seen; the left showed slight venous congestion. The left pupil was large and reacted poorly to light and accommodation. There was ptosis of the right upper lid and exophthalmos, with limitation of ocular movements in the horizontal plane, more on the right; anesthesia in the distribution of the right fifth nerve and slight weakness of the right seventh of the lower neuron type. Hearing was normal. The tongue deviated slightly to the right. The abdominal reflexes were normal. The knee reflexes were absent; the ankle reflexes were present. There was no Babinski sign, although the left plantar response was at times equivocal. Kernig's phenomenon was absent. There was generalized wasting with hypotonia. There was no ataxia. Sensation as far as could be tested was normal. There was no evidence of sinusitis. The spinal fluid was bloody and under increased pressure. The Wassermann test was negative in both blood and spinal fluid. The roentgen-ray examination of the skull showed evidence of increased intracranial pressure, the coronal and lambdoidal sutures being pronounced. Erosion of the posterior clinoid processes was present. The floor of the sella was depressed. The white cell count was 10,400, with 5 per cent. polymorphonuclear cells. The Pirquet test was negative. Operation was refused.

The postmortem findings in the skull were as follows:

Brain: The calvarium was removed without difficulty and was somewhat thin. The dura stripped readily. The brain appeared large for a child of 11 years. The convolutions were somewhat flattened on both sides. The brain was removed with difficulty. At the base of the brain there was an irregular mass of material which seemed somewhat friable and contained plaques varying in size, most of them about 1 mm. in diameter. This tissue was spread over the brain stem, the pons and the pyramids and extended backward to the cerebellum and into the interpeduncular space; it appeared to be attached to the tissue filling the sella. On opening the latter it was found to contain a mass of tissue which was somewhat blood stained and mixed with blood clot. The latter extended forward into the ethmoid cells on the left, but there was no communication with the nasal cavity on the other side. There was marked erosion of the sella, also of the torcula. There were small areas of erosion over each temporal bone. There were one or two plaques on the lateral surface of the cerebral hemispheres.

The right orbital fossa was somewhat large. On dissection of the right eyeball it was seen to contain an increased amount of vitreous humor; otherwise it appeared normal. The final pathologic diagnosis has not yet been made.

The dominant findings in the case are those of middle fossa lesion on the right (ocular muscle palsies, anesthesia in the distribution of the fifth with resulting neuroparalytic keratitis and conjunctivitis). There were slight evidences of extension of the process posteriorly (peripheral facial palsy and slight deviation of the tongue). There was also an apparent lesion of the internal fibers of the third nerve on the left, but the findings, with the exception of those pointing to the lesion of the right middle fossa, were meager indeed when one considers the widespread character of the lesion. It is worth noting that there was no evidence of choked disk. This may have been due to the yielding of the sutures noted in the roentgen-ray report. That intracranial pressure was increased was shown by the roentgen-ray findings

in the skull, the increased tension in the lumbar fluid, and possibly also the diminution of the knee reflexes. The last is commonly seen in cases of hydrorrachia. The alternative explanation for the diminution of the patellar reflexes, that of possible injury to the cerebellar pathways, could not be demonstrated, although there was noted hypotonia of the musculature. The bleeding from the nose on the right side led to the consideration for a time of cavernous sinus thrombosis, but this diagnosis was rapidly abandoned. The protrusion of the right eyeball was not adequately explained by the necropsy findings, but it has been noted frequently in middle fossa tumors and may be due to irritation of the sympathetic filaments which innervate the so-called Landstroem muscle surrounding the eyeball.

DISCUSSION

DR. FOSTER KENNEDY: Although Dr. Friedman explained the diminution and absence of deep reflexes in this case as due to the increase of intracranial pressure there was no great evidence of this or of traction on the posterior spinal roots at any time. The tumor has the appearance of a multiple sarcomatosis.

CASE OF INTERNAL COMMUNICABLE HYDROCEPHALUS BEARING ON RECENT EXPERIMENTAL WORK. Presented by DR. I. STRAUSS and DR. J. H. GLOBUS (the latter by invitation).

The patient, a 3 months old child, weighed 6½ pounds (about 3 kg.) at birth, after which the head became progressively enlarged. The child had club feet, the legs were held flexed and in contracture, the arms moved freely. Fluid was removed from the ventricles, and after the removal the fontanelles remained depressed. The child was apparently blind.

The brain exhibited a marked degree of internal hydrocephalus. The cortex of both cerebral hemispheres was reduced to paper thickness. The pons, medulla and basal ganglions appeared normal in size. An India ink injection was made after death into the pontocerebellar system, and the injection went forward as far as the chiasm and covered the cerebellum and the midbrain. None of the injected fluid reached the surface of the hemispheres, nor did it enter the ventricles. An examination of the meninges revealed no evidence of an inflammatory process. It therefore appears that the obstruction in the subarachnoid space was a developmental defect.

Sections through the midbrain also showed rudimentary remains of the aqueduct of Sylvius, so that this case was both an obstructive and communicable type of hydrocephalus.

TERATOID CYST OF THE HYPOPHYSIS (PATHOLOGIC MATERIAL AND LANTERN SLIDES). Presented by DRS. J. H. GLOBUS and I. STRAUSS.

The tumor presented showed in addition to the uncommon histologic structure, features of clinical significance. It occurred in a girl, 6 years of age, who had had no previous illness and who had been quite normal up to the time of the onset of symptoms, six months before admission to the hospital. At that time she became restless, markedly constipated, lost her appetite and developed polydipsia and polyuria. Several weeks later, the diagnosis of diabetes was made, and she was treated accordingly. A week before admission to the hospital the child's mouth was drawn to one side and her left shoulder dropped and frequently twitched. She was admitted to the hos-

pital with the complaint of headache, fatigue, excessive thirst, enuresis, loss of appetite and weakness of the left shoulder.

Physical examination showed a fairly well nourished child, somewhat undersized, with a profuse growth of lanugo hair all over the body. There were found: ptosis of the right eyelid, weakness of the right internal rectus: the left pupil was larger than the right with both pupils reacting to light and accommodation. There were also left facial weakness, slight weakness of the left arm and hand, and slight weakness of the left leg. The deep reflexes were more active on the left side, though generally reduced. Gait and station were normal. The abdominal reflexes could not be elicited. The spinal fluid was negative as regards cells and the Wassermann reaction. The diagnosis of neoplasm involving the posterior lobe of the pituitary and the right crus cerebri was made.

At necropsy a large purple fluctuating mass was found at the base of the brain. It covered the optic chiasm and was adherent to the latter. Posteriorly it filled up the entire interpeduncular space. Its bulging inferior surface, which was partially free, was prolonged into a funnel-shaped process which seemed to be continuous with the pituitary body. The latter was small in size and compressed, and was lodged in a shallow and eroded sella turcica. The base of the superior surface of this mass was firmly implanted in the substance of the basal surface of the brain. It occupied the entire interpeduncular space and, because of pressure on the adjacent structures, the optic chiasm and the optic tracts were flattened. The tuber cinereum and the mammillary bodies could not be identified since the floor of the third ventricle was stretched and flattened by the tumor mass which almost obliterated the cavity of the third ventricle by its protrusion into it. The cerebral peduncles were displaced laterally and, due to pressure, were reduced in size, this being more pronounced on the right side. The neoplasm, which contained a dark brown, granular, semifluid mass, was a rather thin-walled cyst, lined by a corrugated membrane which was studded with numerous small, glistening elevations. The cyst, which was 4 cm. long, 3.5 cm. in width, contained cholesterin crystals. It pressed on and flattened both of the optic nerves and the right oculomotor nerve. A horizontal, longitudinal section of the brain showed the cavity of the cyst fully exposed and that, at the left of the anterior portion, its wall was thickened, giving rise to a tuberous elevation cartilaginous in consistency and somewhat translucent in appearance.

The wall of the cyst was for the most part of a uniform thickness and histologic structure, and was composed of three layers. The innermost coat, a layer of stratified squamous epithelium showed at a few points a little variation in the character and maturity of its epithelium. The middle layer consisted of loose connective tissue in which were imbedded numerous glandular acini and many small ducts. The glands appeared to be salivary in character, and the ducts were lined by tall cuboidal epithelium and filled with a pink staining colloidal substance. The third and outermost layer was composed of a fairly thin stratum of dense fibrous connective tissues forming a boundary between the brain tissue and the cyst and serving as the outer protective wall of the exposed part of the cyst.

The lining epithelium showed its strong resemblance to the epithelium of the dermis of a young embryo by its three layered formation and by the presence of hair germs. Again accumulation of deeply staining epithelial cells in concentric layers gave rise to structures not unlike epithelial pearls. The cells in the center of these pearls appeared to undergo degeneration, the peripheral

cells having retained the structure of basal cell epithelium and showed, when stained specifically, the characteristic intercellular bridges and keratohyaline granules. In the small cartilaginous mass were found several types of embryonic tissue of mesodermal origin, such as embryonal cartilage mucous connective tissue, young fibrous tissue, newly formed bone with typical bone corpuscles, calcified trabeculi, endosteum and periosteum crowded with numerous osteoclasts, osteoblasts, osteophites, and marrow cells filled with yellow granules, which on staining with specific methods gave a typical iron reaction. In addition to these structures, there was a collection of cells arranged in long cords and supported by a fine reticulum, which contained fat and in general strongly resembled cells in sebaceous glands.

The unusual histologic features of the tumor place it among a rather small group of neoplasms, which recently through the work of Erdheim have been traced to misplaced embryonal remnants of the subinvoluted craniopharyngeal duct, though such cysts in the past have been variously described as cholesteatomas, dermoids, epidermoids and occasionally, because of the occurrence of cartilage and bone in their walls, as teratomas.

The confusion in the classification of such cystic neoplasms was due to the fact that some coincidental findings, such as cholesterin crystals, bone or cartilage were accepted as basic and fundamental features of such tumors.

It is most probable that the various tissues found in the neoplasm described were derived from the two germ layers, ectoderm and mesoderm, which make up the mature skin. It is then assumed that the cyst described is a teratoid growth, autochthonous in origin, which was formed by an embryonal misplacement of cells from the two germ layers during the period of the invagination of the ectoderm and in the course of the formation of the hypophysis.

The gross anatomic relations of the tumor to the hypophysis and to the structures in the floor of the third ventricle are of significance in view of the clinical manifestations pointing to a disturbance of pituitary functions. This is particularly true in the light of recent experimental works by Baily and Bremmer, who have shown that the clinical symptoms of diabetes insipidus, such as polydipsia, polyuria and cachexia can be provoked with certainty by a lesion produced in the postinfundibular region of the hypothalamus, while the complete removal of the posterior lobe of the hypophysis does not lead to permanent production of such symptoms.

The tuber cinereum, the mammillary bodies and in fact, the entire floor of the third ventricle was almost completely destroyed through pressure by the tumor mass, while the infundibular portion of the hypophysis showed no change except compression. It would appear that the findings in this case serve to support the results of the experimental work of Baily and Bremmer.

THE BIOLOGIC INTERPRETATION OF PSYCHONEUROSIS. Presented by DR. L. GRIMBERG.

Every psychoneurotic person, if carefully examined, shows some endocrine disturbances as evidences of endocrine maldevelopment. This condition is a prenatal state and forms an organic inferiority, which means that the person in question is a vulnerable person and under certain circumstances will develop a psychoneurosis. The present classification of psychoneurotic persons is made entirely from the psychologic point of view. Even if the freudian theory is accepted, the psychoneurotic person is conceived as a result of a conflict going on in the individual in question, and the compensation which arises in the form of a psychoneurosis is a result of psychologic maladjustment. On the

other hand, a person cannot be conceived as an entity. It is erroneous to look at him otherwise than as a sociologic unit. His illness is defined not so much by his mental state as by his mental attitude. The psychoneurosis is manifested by the relations between the person and other people. It is exactly that point which has been overlooked in the study of psychoneurosis, and the importance of the milieu in the production of psychoneurosis must be considered if we intend to reach to a proper understanding.

Based on the theory of Weissmann (on heredity) every normal person is born with the potentiality to reach the stage in which his parents are and also with the potentiality to overreach that stage. (That determines progress.) This will explain the appearance of atavism, because there it is possible that the molecular structure of the germ cell may be so changed that regression is taking place.

I will explain the nature of the conflict which takes place between the conservative elements transmitted by heredity—egotism and the milieu. The milieu represents all that surrounds the person. Sociologically it is society. Society is formed by conscious elements, but the resultant is not a conscious entity. On the other hand, this resultant of all the conscious elements—society—represents an equilibrium between the conservative factor transmitted by heredity (egotism) and the revolutionary factor (altruism). The normal person is born with the potentiality to reach that compromise, or equilibrium of the social entity from which he springs.

A classification of the psychoneuroses, based on the study of this conflict, will give us a more reasonable and plausible explanation of the appearance of psychoneurosis. Some of the classes of psychoneurotic persons are:

(1) Persons born without the potentiality of compromise. They are usually the amorals of Lombroso, the criminals and sexual perverts.

(2) Persons born with the potentiality of compromise but at the same time the milieu, which comes into conflict with them at the start, like the family, is not in compromise. The result is that egotism instead of shaping itself becomes more pronounced. Or the person is developed into a personality with an exaggerated ego, though with the potentiality and though the milieu is in compromise, but due to various causes, like the only child.

(3) Persons who at one time in a certain milieu were in compromise, but then came into a different milieu and the conflict started anew. As examples we have the racial psychoneuroses in our country.

### DISCUSSION

DR. RUSSELL G. MACROBERT: I would like to ask whether Dr. Grimberg really considers emotional stress or strain, such as fright, grief, worry and chagrin, less important than the character of the glands of the person in determining a psychoneurosis?

DR. FOSTER KENNEDY: Dr. Grimberg's subject embraces so wide a field it would not be possible to discuss it properly in so limited a time. He defines a psychoneurotic as being a person in constant reaction with his milieu. I do not quite know what he means by the use of the word "reaction." If he means conflict with his milieu I can understand it; but reaction is not necessarily conflict. After all, the whole process of life is one of reaction to the milieu, and that is a perfectly normal situation; not at all the abnormal condition of emotion suggested by the use of the word psychoneurosis. Again, Dr. Grimberg said that egotism was unknown among the lower animals. In what sense did he use the word egotism in that remark?

DR. L. GRIMBERG: I use the term egotism in the sense we use it in ethics. I mean conscious sacrifice. Of course there is such a thing as egotism among lower animals. About the other questions, I did not say definitely that the endocrine glands have any importance at all. I made the remark that they might show an organic inferiority of the person. About the reaction I expressed myself badly. I really did mean that the psychoneurotic person is in a continuous state of conflict with his milieu.

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## SAN FRANCISCO NEUROLOGICAL SOCIETY

*Twelfth Regular Meeting, Jan. 13, 1922*

M. B. LENNON, M.D., *President, in the Chair*

PSEUDOTUMOR OF THE BRAIN. Presented by DRS. H. C. NAFFZIGER and G. Y. RUSK.

An Italian, aged 43 years, five years ago began to complain of failing vision, followed by paresthesia of the right side of the body and face. His hearing also became involved, first on the right side and later on both sides. At the same time he suffered with severe frontal headaches for several months, with nausea and vomiting. Three months before admission to the University Hospital he had diplopia, his gait was stumbling and he had occasional dizzy spells. He was mentally confused and his memory was poor.

Physical examination showed that the pupils were equal, regular and reacted to light and distance. The fundi showed swelling of both disks and obliteration of the disk outlines. There was a homonymous hemianopsia and right internal strabismus. The deep reflexes were exaggerated; urine examination was negative, as were also the blood Wassermann and spinal fluid tests. The blood count was normal.

The final decision in this case was a midline growth, but an exploratory operation failed to reveal a pituitary tumor.

Necropsy examination, limited to the brain alone, showed an extensive hemorrhage in the right frontal lobe which was the cause of death. No evidence of the tumor was found. Cutting into the left optic radiation from the ventricular side was a chronic lesion, soft and yellow, which on microscopic examination contained many compound granule cells. On the other side, almost symmetrically placed, was a smaller lesion, apparently a somewhat older process. Section through the pons showed another little focus of softening. In the latter region microscopically could be seen vessels completely occluded. Undoubtedly these foci were embolic in origin. There was no history of heart disease or pulmonary condition which might account for the emboli, however. It is interesting in this case that there was choking of the disks. There was no evidence of chronic syphilis to account for the headaches. While the roentgen ray apparently showed almost complete destruction of the anterior clinoids and some erosion of the posterior clinoids, necropsy failed to substantiate these findings.

DIFFUSE CEREBRAL SCLEROSIS. Presented by DR. G. Y. RUSK.

The patient was an infant of 17 months; a full term child, whose birth was normal, although labor was prolonged. The first tooth appeared at 9

months, and the fontanels closed at 9 months. The child never sat up, never talked and never recognized its mother. There was no reaction to light or sound.

All the reflexes were exaggerated and examination revealed general spasticity. The right leg suddenly became flaccid three weeks prior to death. All laboratory reports were negative.

At necropsy there was found marked external hydrocephalus. The brain showed marked general atrophy. The cortex was universally firm; the convolutions narrow and the sulci wide. Considerable pressure with a razor blade had to be used in order to cut out the sections. The basal ganglions were relatively normal in size. Numerous sections were taken from one hemisphere and the cord. The flaccid paralysis was explained by a definite ventral horn lesion—histologically, anterior poliomyelitis. Cortical sections showed that the nerve cells were relatively greatly reduced with diffuse glial hyperplasia.

To summarize: The condition was a diffuse sclerosis affecting the cortex, while the basal ganglions were relatively intact. Likewise the changes in the cord appeared to be largely secondary to the cortical changes. Necropsy of the lungs showed subacute miliary tuberculosis, and the inflammatory focus in the ventral horn might have been an early embolic tuberculous process.

## BRAIN TUMORS WITHOUT MANIFESTATIONS OF INTRACRANIAL PRESSURE. Presented by Dr. H. C. Naffziger.

(A report from the division of neurological surgery at the University of California Hospital on brain tumors without manifestations of intracranial pressure.)

There were presented seven consecutive cases, in all of which two years had elapsed since operation. The economic status of these after operation was given and compared with the results of operation in cases showing ophthalmoscopic and other signs of intracranial pressure at the time of operation.

All of the patients in the cases reported have returned to the same work they did prior to operation. Four of them had complete tumor or cyst removals. All of these but one had been incapacitated for work prior to treatment. Of the seven two had infiltrating tumors of the motor region. These were reported in detail.

A man, aged 48, presented paralysis of the left arm and leg with striking atrophies of these extremities. He had jacksonian and general convulsions. Following a radical removal of the growth—an infiltrating glioma 4 by 4 by 2 cm.—power gradually returned in the formerly paralyzed extremities. In six months this patient returned to manual labor and has now continued work for two years without signs of a recurrence. The general convulsions have ceased, and infrequent minor attacks have been controlled with phenobarbital (luminal). The second patient, a man aged 35, presented a complete paralysis of the left arm, with jacksonian attacks. Following a radical removal of a glioma of the small cell type measuring 3 by 2.5 by 1.5 cm., power began to return in the arm in three weeks. In eight months all movements could be performed. The grip became 75 per cent. of normal. There was some awkwardness of the finer hand movements, but this was barely noticeable. This patient has been at work as a contractor for over one year.

The absence of any operative mortality in this group of cases, an average post-operative hospital stay of three weeks, and the restoration of all patients to positions as wage earners is a striking improvement over the results in a

far larger group of tumor cases in which the patients first presented themselves for treatment with marked pressure manifestations. Concerning the two having radical removals of gliomas with a margin of normal tissue it is appreciated that the time is too short to indicate permanent cure. With small infiltrating growths radical removal is advocated and a location of the growth in the motor region is not considered a contraindication to this removal. A comparison of successive groups of tumor cases treated which shows an increasing proportion of persons restored to a measure of usefulness is an index of progress in diagnostic and operative treatment.

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## CHICAGO NEUROLOGICAL SOCIETY

*Regular Meeting, Jan. 19, 1922*

LEWIS J. POLLOCK, M.D., *in the Chair*

### A CASE OF DYSTONIA MUSCULORUM DEFORMANS. HUGH T. PATRICK.

This boy of German-Scotch, not Jewish, parentage, nearly 11 years old, was one of twins born at full term after normal labor and no asphyxia. The family history was negative except that the twin brother died at 6 years of a cerebellar glioma. The patient was the larger twin but developed slowly, not talking plainly until 3 years or older. He walked at the proper age and normally until his present trouble began. Progress in school was retarded, partly on account of his present trouble. His mental age was about 8. He had the ordinary diseases of childhood and vomited frequently until the age of 4.

When about 6 it was noticed that he walked and ran peculiarly. In the early summer of 1918, when between 7 and 7½ years of age he began to walk and stand with the body bent forward, due chiefly to flexion of the trunk on the thighs; this was his attitude when I first saw him, Oct. 8, 1918. He was then 7 years and 8 months old. This stooping varied in degree but was constant, and in walking he generally supported the trunk by pressing the right hand against the thigh. But not only could he walk and run without so supporting himself, he could also stand quite straight and walk and run well and normally erect. Two months before blood Wassermann tests on the boy and the mother had been negative. I could make no diagnosis. For two weeks the boy had been having headaches and one naturally thought of brain tumor, but all the ordinary signs were lacking. All extremities were rather clumsy, more so on the right, but the results of examination were practically negative.

I did not see the patient again until Jan. 3, 1922. In the meantime he had been examined by three neurologists, two pediatricians and an internist, and another Wassermann test had been negative. No one made a diagnosis of dystonia musculorum. In July, 1919, one of the neurologists is said to have made a diagnosis of hysteria and cerebral palsy. The boy was sent to a relative in the country and is said to have improved, but by December, 1919, was again worse, stumbling and often falling. In January, 1920, the neurologist saw him again, reaffirmed his diagnosis, and the boy again went to the country. With more or less fluctuation in his condition he gradually grew worse. Since the middle of October, 1921, he has had difficulty in sitting and

for about two and a half months has not been known to sit. When he attempts to do so, the trunk stiffens, then curves backward, the thighs, especially the right, are rigidly extended, the feet twist and if he persists in the attempt eventually he slides from the chair to the floor (Fig. 1). Consequently he stands all day; but he cannot stand quite still; there is a constant slight or moderate writhing movement of the trunk which tends to hyperextension, a little swaying ,and constant unobtrusive shifting from one foot to the other. The arms, too, are in almost constant, slow, slight, restless, rather vermicular movement (Fig. 2).

Fig. 1.—Attempt to sit upright.

For six or eight weeks the boy has been unable to lie down. When he tries to do so the body and limbs stiffen; there are the rather slow writhing movements; the tonic spasm becomes severe; the face flushes; respiration is more shallow and irregular, and gradually he becomes opisthotonic (Fig. 3). Consequently he sleeps in a most bizarre attitude. He kneels in bed, places a pillow between abdomen and thighs and stoops forward until the head rests on another pillow (Fig. 4). Often after going to sleep in this posture he

Fig. 2.—Attempt to stand upright with feet together.

Fig. 3.—Attempt to lie on the back.

falls onto the side and continues so to sleep if undisturbed. At first the mother would try to straighten him, the spasm would return and he would again have to assume the kneeling posture to go to sleep.

In spite of the intense opisthotonic spasm, when I quickly turned the boy onto his side I was easily able to flex thighs and legs. It is such peculiarities as this which often have led to a diagnosis of hysteria. However, this flexion lasted only a moment; the extensor spasm quickly reappeared.

In spite of these peculiar disabilities he can walk well and even run well and does all the ordinary coarser things with the hands: feeds and dresses himself. When asked to stand and stretch out the arms in front of him with fingers spread, he showed slow, very spastic, rather athetotic but slight irregular movements of the arms, forearms and fingers; the trunk muscles contracted more on the right and the right buttock more than the left.

The patient complains a good deal of headache, principally on the right side but otherwise is cheerful, of good disposition, amenable, eats well and complains very little of fatigue.

Fig. 4.—Position in which patient sleeps.

Results of the examination were practically negative. On account of the rigidity and movements examination of both deep and superficial reflexes was very unsatisfactory, but apparently they were normal. The cornea were normal and percussion indicated normal liver dulness. At this time the diagnosis seemed to be easy.

In this connection I might mention a very similar case seen with Dr. Schott in September, 1913. That boy also was 7 years old, and the trouble began in the right leg, which he constantly carried flexed at the knee and hip. This contracture showed the inconstancy and inconsistency which so frequently in these cases has led to a diagnosis of hysteria. The boy could not voluntarily extend hip or knee, and there was resistance to passive extension. He walked with what might be called a typical hysterical gait. With knee and hip flexed but foot extended, he rather slowly advanced the right foot until the tip of the toe touched the floor and then hopped forward with the left leg. When I asked him to turn a childish somersault he readily did so, and in the act the hip and knee straightened out in a perfectly normal way. I made a diagnosis of hysteria, but later had an opportunity to reverse my decision. I showed the boy at the meeting of the American Medical Associa-

tion in Detroit, when there could be no doubt that the case was one of dystonia musçulorum.

In his recent monograph Hall (book review in this issue of the ARCHIVES OF NEUROLOGY AND PSYCHIATRY) classes this disease with progressive lenticular degeneration (Wilson) and pseudosclerosis (Strümpell) and would designate the group "hepato-lenticular degeneration." There have been only two recorded necropsies in dystonia musculorum, and as neither case was a quite typical one, the pathology may still be considered as not definitely settled.

The condition of this boy has been considerably alleviated by relatively large doses of hyoscin (1/100 grain three times a day), which he tolerates exceedingly well.

DISCUSSION

DR. FRANK SMITHIES: When I saw the boy in the summer of 1918 I thought his case was exceedingly interesting and unusual. Our notes indicate a diagnosis of tumor at the base of the brain, passing back toward the medulla. The gait was shuffling and erect station was maintained with difficulty. He could not stand on one foot. After walking 30 or 40 feet (9.12 or 12.16 meters) he stooped forward, pressing his hands on his thighs. In getting up from the recumbent position he progressed fairly well to the sitting posture and fairly well to his feet, but to become erect he climbed with his hands on his thighs, particularly on the right side. The Wassermann reaction was negative on the patient and his mother; the father was not tested. The fundi of both eyes were definitely engorged and edematous. Roentgenographic examination showed an enlarged thymus. There were no signs of pressure; the spine was normal; the hip joint surface was thickened, especially on the left. There was definite irregularity and some erosion of the head of the femur. The skull laterally showed a very small sella and an anomalous basal skull contour. We thought this was indicative of some anomaly at the base of the brain. I saw him in consultation with another physician and made the diagnosis of tumor, largely from the physical findings, the roentgenogram and because his twin brother had had a glioma.

DR. LEWIS J. POLLOCK: I saw this boy about a year and a half ago, and the hyperkinesia was then very slight. One striking feature was exaggeration of the position described by Dr. Smithies, namely, the inability to assume an erect position from the prone except by assistance of the arms as seen in progressive muscular dystrophy—which condition I thought it was. It is exceedingly interesting to note the type of spasm which occurs in these cases. They are more or less homologous to those of torticollis. I recall one case which began as a torticollis. The movements then spread to the rest of the body, and those of the head became so marked that the patient rubbed off all the hair on the back of her head.

Strikingly suggestive of the pathogenesis of such disorders is a case which I saw of a hemiathetosis following a hemiplegia as the result of a thrombosis, which occurred in a woman 39 years old. Accompanying the typical unilateral athetosis was a marked torsion spasm of the opposite sternocleidomastoid. I believe this was due to a lesion in the lenticular nucleus.

DR. DAVID M. LEVY: We made a test which might be of interest because the boy was examined by the Child Study Department. He did not get beyond the first grade in school. In the other cases reported in the literature a notation is made of no intelligence defect, although in the cases reported by Wimmer he recites a number of mental disturbances. This boy rates 8 years by the Stanford Binet test, which should enable him to do third grade work,

but he does not get beyond the first grade. He is classified by the test in the subnormal group, not feebleminded. Another interesting thing the mother told me was that the psychologist who examined the boy made quite a good deal of the fact that he would not dress himself. Not knowing anything about the pathology of the physical disability, he thought the whole thing was to be attributed to his being mentally defective.

## A CASE SHOWING FACIAL DIPLEGIA. Dr. John Favill.

A laborer, aged 41, entered Cook County Hospital, Dec. 31, 1921. His family and his past history were unimportant. There had been no recent use of alcohol, no diphtheria and no gastro-intestinal or other evidence of poisoning.

The present illness probably dated from about the middle of October, 1921, at which time he had a chancre. He stated that a blood Wassermann reaction was positive and that he received nine injections of silver arsphenamin at the Central Free Dispensary. The lesion healed after the third injection. No secondary infections have appeared. About the middle of December, after three days' work shingling a house in very cold weather, he noticed pain in the left side of his face. Earache, tinnitus and gradual loss of hearing set in on the right. In about a week—just a week before entering the hospital—he noticed the facial paralysis. He could not expectorate or close his eyes. Both sides were apparently affected at the same time. The earache was relieved by hot applications, and no discharge occurred. There was some dizziness when walking but no sense of whirling when lying down. He did not vomit and could sleep well.

General examination revealed nothing important. The blood pressure was: systolic 150, diastolic 110. Temperature, pulse, respiration and urine were normal.

The gait was slightly ataxic, coordination fair. No paralyses other than the facial were noted. All reflexes were present and normal, with the exception of rather lively but equal knee reflexes. Sensation was normal for pain, touch, temperature and deep sensibility.

Cranial Nerves: The first nerve was normal. There was diminished vision on the left as the result of an old corneal scar. The left pupil was slightly irregular. Both eyes reacted normally to light, consensual and accommodation tests. The fundi were normal. There was mixed astigmatism. The third, fourth and sixth nerves were normal. The fifth nerve, sensory division, was normal, but the motor division showed weakness of the left temporal and masseter. They responded, however, to the faradic current. The left pterygoids were weak, the jaw deviating somewhat to the left on opening. The jaw reflex was present. The seventh nerve showed complete paralysis of muscles of expression. We could obtain no response in the upper group from the faradic or galvanic current. Stimulation of nerves and muscles in the lower group by the faradic current gave no response, but the galvanic current caused a slow contraction. On the right the cathodal closure contraction equaled the anodal closure contraction, but on the left the anodal closure contraction exceeded the cathodal closure contraction. Taste was certainly impaired if not quite lost in the anterior and middle thirds of the tongue on both sides. The patient said there was dryness in the left half of the mouth. The eighth (cochlear) nerve showed marked deafness on the right, moderate on the left. The canals, membranes and mastoids were normal. Weber's test showed lateralization to the left. The Rinné test was negative on both sides. The Schwabach test showed shortening. Galton's test on the right was 15,000 to

1,024, on the left 18,000 to 32. The eighth (vestibular) nerve showed no spontaneous nystagmus or past pointing. The results of horizontal canal tests were: Right turning gave nystagmus to the left 18 seconds but no past pointing; left turning gave no nystagmus or past pointing. Caloric tests had no effect on either side. The ninth, tenth and eleventh nerves were normal. The twelfth showed slight weakness on the left. The tongue protruded slightly to the left but could be moved in all directions. It showed no atrophy.

Laboratory Findings: The Wassermann reaction was positive on both the blood and spinal fluid. The colloidal gold reaction was 5555431000.

For the past two weeks the patient has been treated with mercury, arsenic, potassium iodid and one injection of neo-arsphenamin. There has been no apparent improvement.

The etiologic diagnosis is somewhat obscure. If we consider this a bilateral Bell's palsy from, say, exposure to cold, it would explain the facial paralysis, the impairment of taste, and the eighth nerve weakness, but we would not expect an involvement of the left fifth or twelfth nerve. If we consider a syphilitic basilar lesion, it would explain all the positive findings, including taste impairment, providing we assume that at least a part of taste is transmitted along the nervus intermedius from the geniculate ganglion to the brain stem. It is strange, however, if this is of syphilitic etiology, that there have been no headaches, no sixth nerve trouble, no optic disk changes and no improvement from treatment.

DISCUSSION

Dr. Hugh T. Patrick: Some years ago I reported a facial diplegia as the principal indication of multiple neuritis following slight infection and at that time found that probably bilateral Bell's palsy is of the same nature. That is, it is degenerative, not really inflammatory, and due to an infection, assuming exclusion of syphilis, tumor, etc. Dr. Favill's case seems to be one of these—with a little added.

I would suggest that Dr. Favill reexamine the superior seventh nerve with the galvanic current. There should be contraction with direct stimulation of the muscle. It is impossible that galvanic irritability could disappear in seven or eight weeks.

The loss of taste in the anterior half of the tongue practically settles the localization, because there is only one part of the nerve accompanied by the chorda tympani. Wherever else the lesion may be, it must involve the part of the nerve in the petrous portion of the temporal bone.

Dr. A. B. Yudelson: Was there any disturbance of deglutition?

Dr. George W. Hall: I had occasion some time ago to read an article by Carl von Rad (A Case of Facial Diplegia with Ophthalmoplegia Externa, Deutsch. Ztschr. f. Nervenh. **17**:209) on involvement of the cranial nerves of infectious origin without involvement of the other peripheral nerves. He reported one case in a boy of 15 years with facial diplegia coming on suddenly with almost simultaneous involvement of the third, fourth and sixth nerves on that side, producing extreme ophthalmoplegia. The condition cleared up entirely within four and a half months. He quotes many other cases involving the fifth nerve, which were put on the basis of being peripheral nerve involvement and not nuclear involvement.

Dr. H. Douglas Singer: I should like to ask the degree of intensity of the Wassermann reaction in the spinal fluid and whether sufficient blood was

present to account for this reaction. Is it not possible that the two conditions can be combined; that is to say, that there is a multiple neuritis of syphilitic origin, a toxic degeneration of the nerves due to syphilis?

DR. FAVILL (closing the discussion): There was no disturbance in deglutition at any time. The patient says that for a long time he has preferred to chew on the right side, which may denote a long standing weakness in the left fifth nerve, or the muscles which it supplies.

My suggestion of a basilar lesion accounting for the taste impairment was made in the belief that some taste is transmitted by the nervus intermedius, which with the seventh and eighth nerves could be caught central to the internal auditory meatus. I do not know whether it is differentiated which form of taste goes this way and which the other. However, even if all taste fibers from the anterior tongue leave the facial canal from the geniculate ganglion, along the great superficial petrosal, to join the middle sensory branch of the fifth nerve, they still have to cross the base of the brain to get into the brain stem and, I should think, might be affected then.

The determination of the degree of the Wassermann reaction is usually not given in the county hospital laboratory reports, and I cannot state what the number of "plus" was. The record stated that microscopic blood was present. There were about four red cells to the field, which probably would not produce that result.

MULTIPLE SOFTENING VERSUS MULTIPLE SCLEROSIS. G. B. HASSIN and PETER BASSOE.

(To appear as an original communication in the ARCHIVES OF NEUROLOGY AND PSYCHIATRY.)

# Book Review

LA DEGENERESCENCE HEPATO-LENTICULAIRE. MALADIE DE WILSON—PSEUDO-SCLEROSE. Par H. C. HALL, Ancien Chef de clinique á l' "Hospital de Bispebjaerg," Copenhague, Chef de laboratoire de l'Institut Sérothérapique de l'Etat Danois. Preface du PROF. PIERRE MARIE. Price, 20 francs Pp. 360. Paris, 1921.

This brochure, a translation from the Danish, is the most extended review of Wilson's disease, pseudosclerosis and cognate maladies which has appeared, being much more detailed than the monograph of Stertz (ARCHIVES NEUROLOGY AND PSYCHIATRY **6**:357 [Sept.] 1921), which, by the way, receives no notice from Hall.

In the first two chapters, forty-four pages, the author gives a sketch of progressive lenticular degeneration as a morbid entity and outlines the development of our knowledge of this disease and of pseudosclerosis and of the gradual tendency to correlate the two as closely related, if not identical, diseases.

Chapter 3, seventy-three pages, relates the exceptional personal experience of the author. He had carefully examined four patients and reports three additional cases reported to him by others. One of his own cases is clinically reported in full; it then came to necropsy which was complete, including detailed microscopic study of the central nervous system, abdominal and thoracic organs and the cornea. Characteristic lesions were found in the brain, liver and cornea. His patients showed the familial tendency of the disease. This chapter is illustrated by excellent photomicrographs and photographs.

The author then tabulates (Chapter 4, twenty-four pages) sixty-eight cases of Wilson's disease and pseudosclerosis reported since 1912, including his own.

Symptomatology is methodically covered (sixty pages) and pathologic anatomy fully detailed (fifty-four pages), including an exhaustive study of the corneal pigment found in many of these cases. The author then groups progressive lenticular degeneration (Wilson's disease), pseudosclerosis (Westphal-Strümpell) and dystonia musculorum deformans (Oppenheim) or the torsion spasm of Ziehen as three types of one disease, which he proposes to designate hepatolenticular degeneration.

In Chapter 9 the author considers various striate syndromes, six in number: Wilson's disease (with pseudosclerosis and torsion spasm), Huntington's chorea, double athetosis, paralysis agitans, juvenile paralysis agitans, and vascular, syphilitic and neoplastic lesions in the striatum.

Chapter 10 is devoted to pathologic physiology, Chapter 11 to differential diagnosis and Chapter 12 to etiology. Seven pages of conclusions terminate the book proper, but this is followed by an appendix noting some recent publications and an extensive bibliography. The monograph as a whole is an excellent piece of work, may well guide subsequent workers, and will save any one investigating the subject an enormous amount of bibliographic research.

Perhaps it is pertinent to add that while Pierre Marie contributes a frankly laudatory preface, he quite as frankly avows reservation as to the preponderant

rôle played by the corpus striatum in the morbid groups described in this brochure. He doubts that the researches of Hall and others have determined the functions of the striate body and the character of symptoms resulting from lesions of this body. One of the chief reasons for these doubts rests in the symptomatology of what he and his pupils, Catola and Ferrand, have described as "cerebral lacunae of disintegration." In this *état lacunaire* the lenticular nuclei especially are often the seat of obvious multiple lesions, and yet the clinical picture is widely different from that of this so-called striatum group.